INVENTOR SEARCH

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=> fil capl; d que nos l26
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FILE COVERS 1907 - 10 Mar 2009  VOL 150 ISS 11
FILE LAST UPDATED: 9 Mar 2009  (20090309/ED)

Caplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

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This file contains CAS Registry Numbers for easy and accurate
substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L1              STR
L2          119 SEA FILE=REGISTRY SSS FUL L1
L18          73 SEA FILE=CAPLUS SPE=ON  ABB=ON  JOHANNES C?/AU
L19       59001 SEA FILE=CAPLUS SPE=ON  ABB=ON  LI X?/AU
L20          12 SEA FILE=CAPLUS SPE=ON  ABB=ON  PESANT M?/AU
L21       13399 SEA FILE=CAPLUS SPE=ON  ABB=ON  ZHAO H?/AU
L22         644 SEA FILE=CAPLUS SPE=ON  ABB=ON  AKASAKA K?/AU
L23        2248 SEA FILE=CAPLUS SPE=ON  ABB=ON  FANG F?/AU
L24         356 SEA FILE=CAPLUS SPE=ON  ABB=ON  GALLAGHER B?/AU
L25         130 SEA FILE=CAPLUS SPE=ON  ABB=ON  L2
L26           4 SEA FILE=CAPLUS SPE=ON  ABB=ON  L25 AND (L18 OR L19 OR L20 OR
                L21 OR L22 OR L23 OR L24)


=> d ibib abs hitstr l26 1-4

L26  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2007:658431  CAPLUS  Full-text
DOCUMENT NUMBER:         147:226508
TITLE:                   In vitro and in vivo anticancer activities of
                         synthetic (-)-laulimalide, a marine natural product
                         microtubule stabilizing agent
AUTHOR(S):               Liu, Junke; Towle, Murray J.; Cheng, Hongsheng;
                         Saxton, Philip; Reardon, Cathy; Wu, Jiayi; Murphy,
                         Erin A.; Kuznetsov, Galina; Johannes, Charles
                         W.; Tremblay, Martin R.; Zhao, Hongjuan
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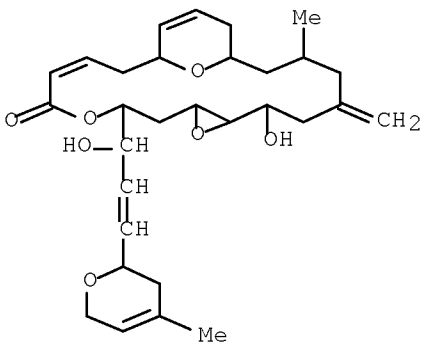
; Pesant, Marc; Fang, Francis G.;
Vermeulen, Mary W.; Gallagher, Brian M., Jr.
; Littlefield, Bruce A.
CORPORATE SOURCE: Eisai Research Institute, Andover, MA, 01810, USA
SOURCE: Anticancer Research (2007), 27(3B), 1509-1518
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Laulimalide is a cytotoxic natural product isolated from marine sponges. It is structurally distinct from taxanes. However, like paclitaxel, laulimalide binds to tubulin and enhances microtubule assembly and stabilization. It exhibits potent inhibition of cellular proliferation with IC50 values in the low nM range against numerous cancer cell lines. In contrast to paclitaxel, however, laulimalide is also very potent against multidrug-resistant (MDR) cancer cell lines which overexpress P-glycoprotein (PgP). It has unique structural and biol. properties, and attempts at synthesis have attracted considerable effort in recent years, resulting in more than ten published total syntheses. Despite this extensive attention, there have been no reported in vivo evaluations of laulimalide to date, probably due to the structural complexity of laulimalide and the scarcity of natural material. In our studies to explore the therapeutic potential of laulimalide, a total synthesis capable of producing gram quantities of laulimalide was designed, which enabled both in vitro and in vivo evaluation. Our in vitro results with synthetic material confirmed the previous reports that laulimalide is a mitotic blocker that can inhibit the growth of a variety of both non-MDR and MDR human cancer cell lines. However, despite demonstrating promise in cell-based and pharmacokinetic studies, laulimalide exhibited only minimal tumor growth inhibition in vivo and was accompanied by severe toxicity and mortality. The unfavorable efficacy to toxicity ratio in vivo suggests that laulimalide may have limited value for development as a new anticancer therapeutic agent.

IT 115268-43-4, (-) Laulimalide
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
((-)-laulimalide inhibited growth of human cancer cells for breast cancer, histiocytic lymphoma, prostate cancer, fibrosarcoma with P-glycoprotein but minimal inhibition in mouse with breast cancer cells with severe toxicity and mortality)

RN 115268-43-4 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

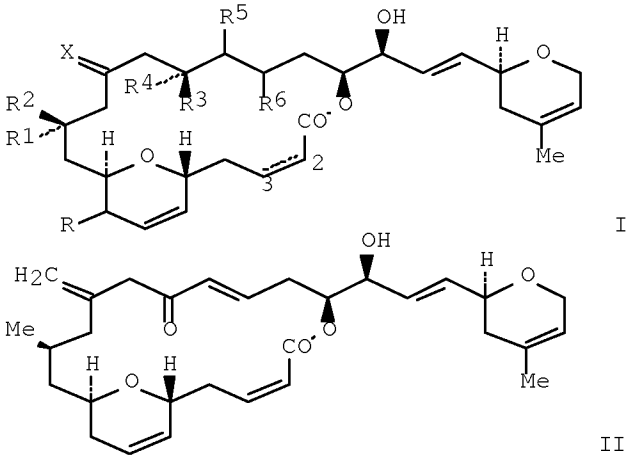


REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:300455 CAPLUS Full-text
DOCUMENT NUMBER: 142:373607
TITLE: Preparation of laulimalide analogs for use in pharmaceutical compositions as chemotherapeutic, antiproliferative, anticancer agents
INVENTOR(S): Gallagher, Brian; Johannes, Charles ; Li, Xiang-yi; Pesant, Marc; Zhao, Hongjuan; Akasaka, Kozo; Fang, Francis G.
PATENT ASSIGNEE(S): Eisai Co. Ltd., Japan
SOURCE: PCT Int. Appl., 227 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005030779	A2	20050407	WO 2004-US31076		20040922
WO 2005030779	A3	20080124			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA					
US 20070287745	A1	20071213	US 2007-572870		20070509
PRIORITY APPLN. INFO.:			US 2003-505354P	P	20030923
			WO 2004-US31076	W	20040922

OTHER SOURCE(S): CASREACT 142:373607; MARPAT 142:373607
GI



I

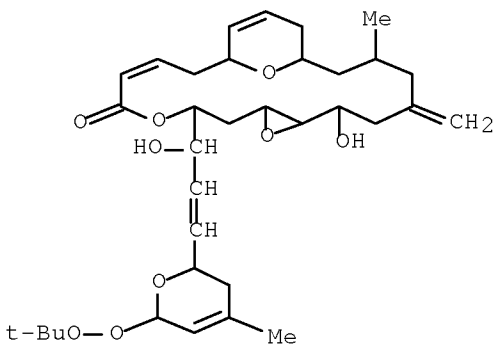
II

AB Laulimalide analogs, such as I [R = H, OMe; R1 = H, R2 = Me; R1 = R2 = H; R3 = H, R4 = OH; R3 = OH, R4 = H; R3R4 = :O; R5R6 = bond, -O-; 2,3-bond = single, double, triple], were prepared for therapeutic uses in the treatment of cancer and other disorders associated with cellular hyperproliferation. These laulimalide analogs are claimed for use as inhibitors of the growth of multidrug resistant cells and for use in combination with an addnl. cytotoxic agent, with an anticancer agent, such as paclitaxel, with an anti-inflammatory agent, or with an agent for treating psoriasis and/or dermatitis. Thus, laulimalide analog II was prepared via a multistep synthetic sequence. The prepared laulimalide analogs were tested for cytotoxicity against human fibroblast IMR-90 cells, against SK-OV-3 human ovarian carcinoma cells, against U937 lymphoma-monocyte-like cells, and against human uterine sarcoma cell lines MES-SA, the MDR neg. parental cell line, and Dx5-Rx1, a cell line derived from MES-SA after long term of exposure to doxorubicin.

IT 849525-26-4P, ER 808455
RL: BYP (Byproduct); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of laulimalide analogs for use in pharmaceutical compns. as chemotherapeutic, antiproliferative, anticancer agents)

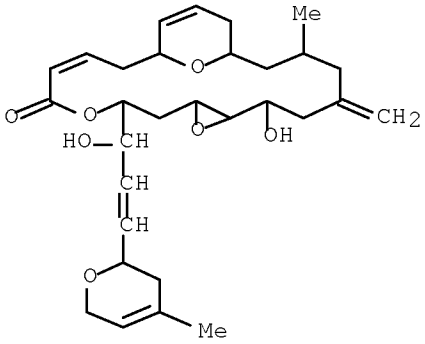
RN 849525-26-4 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-6-[(1,1-dimethylethyl)dioxy]-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



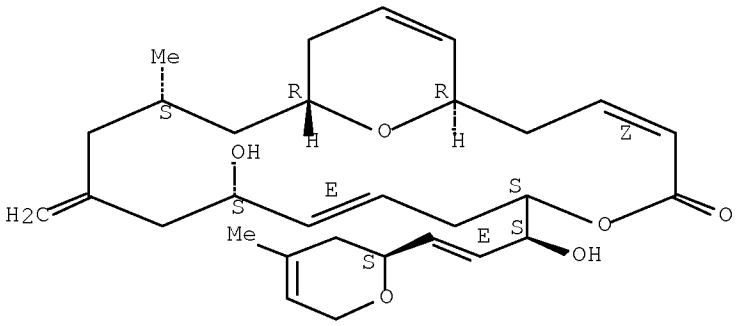
IT 115268-43-4P, ER 806782 352208-15-2P, ER 805886
676474-07-0P, ER 808572 849520-77-0P, ER 808574
849520-78-1P, ER 808575 849526-23-4P, ER 809172
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of laulimalide analogs for use in pharmaceutical compns. as chemotherapeutic, antiproliferative, anticancer agents)

RN 115268-43-4 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 352208-15-2 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

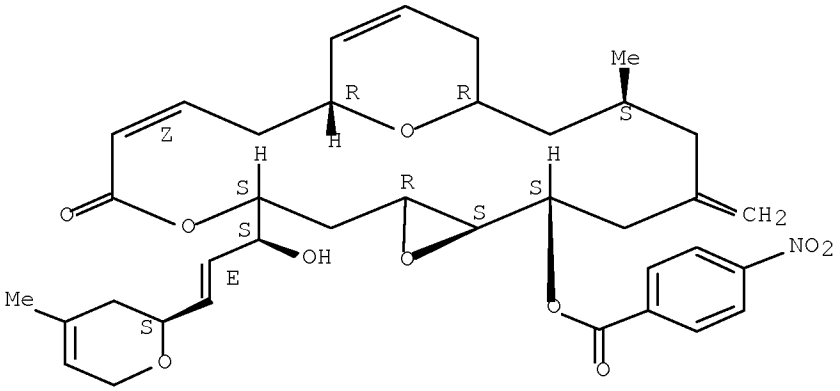
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



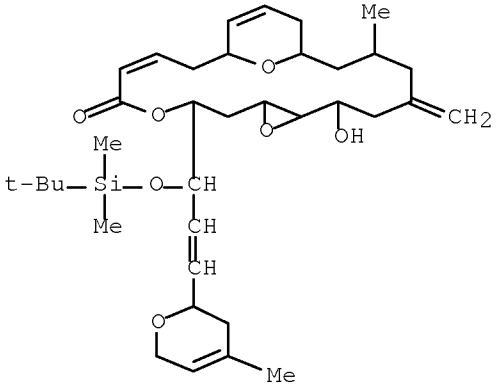
RN 676474-07-0 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-3-methyl-5-methylene-7-[(4-nitrobenzoyl)oxy]-,

(1R,3S,7S,8S,10R,12S,15Z,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 849520-77-0 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



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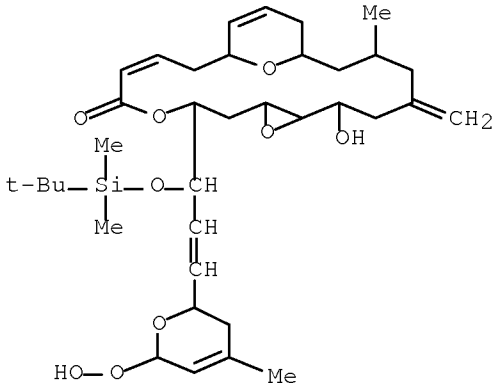
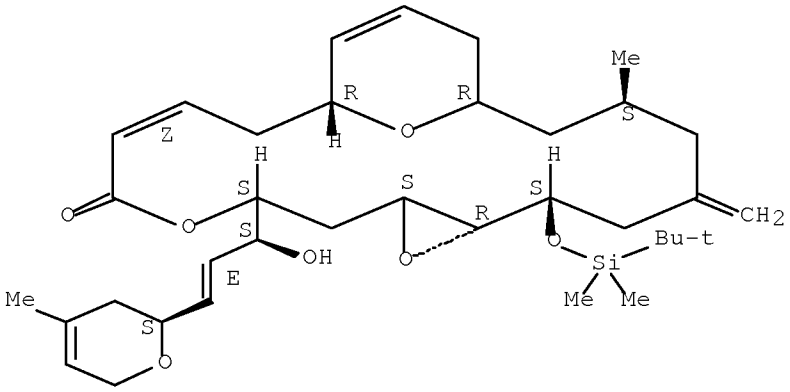


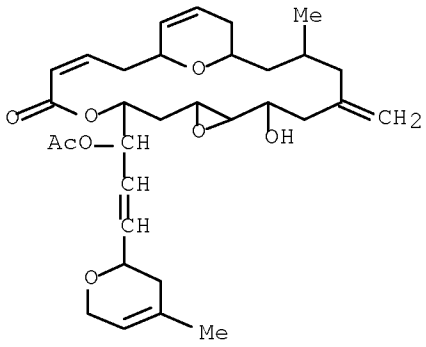
RN 849526-23-4 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-7-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 352208-18-5P, ER 808546 352208-19-6P, ER 807397
385809-27-8P, ER 805883 449180-74-9P, ER 809539
676473-87-3P, ER 805885 676473-89-5P, ER 805884
676473-91-9P, ER 807308 676473-94-2P, ER 808545
676473-97-5P, ER 808715 676473-99-7P, ER 808716
676474-01-4P, ER 808860 676474-03-6P, ER 809173
676474-04-7P, ER 809170 676474-05-8P, ER 808550
676474-06-9P, ER 808547 676474-26-3P, ER 808626
849362-19-2P 849524-67-0P, ER 807129
849526-27-8P, ER 807318
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of laulimalide analogs for use in pharmaceutical compns. as chemotherapeutic, antiproliferative, anticancer agents)
RN 352208-18-5 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one,

12-[(1S,2E)-1-(acetyloxy)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)-(9CI) (CA INDEX NAME)



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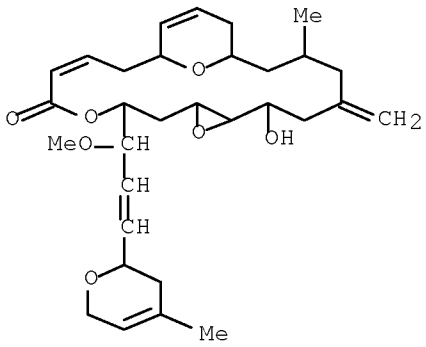
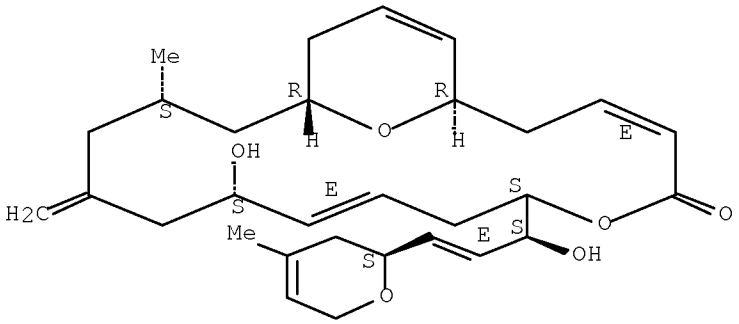


RN 385809-27-8 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3E,7S,9E,11S,15S,17R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 449180-74-9 CAPLUS
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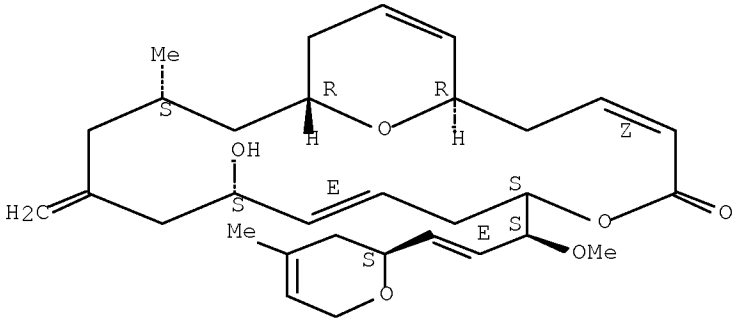
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 676473-87-3 CAPLUS
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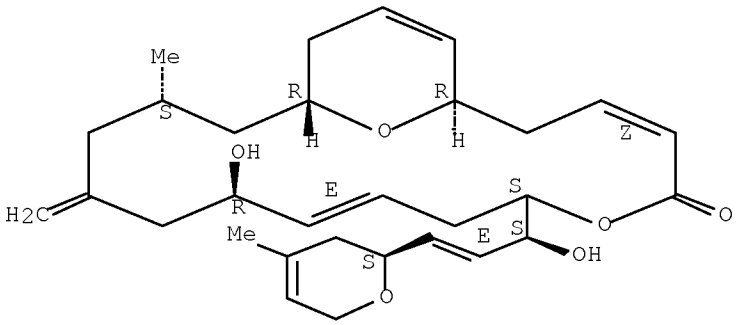
Absolute stereochemistry.
Double bond geometry as shown.



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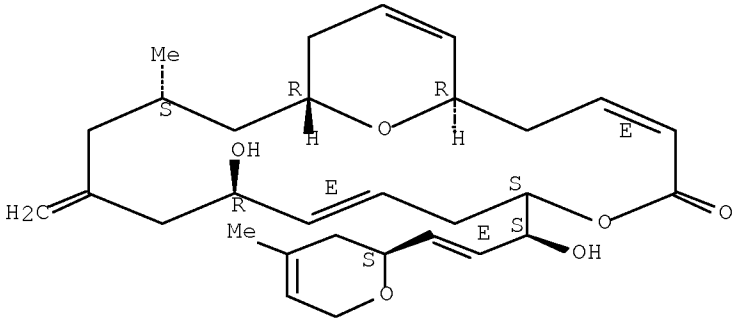
Absolute stereochemistry.
Double bond geometry as described by E or Z.



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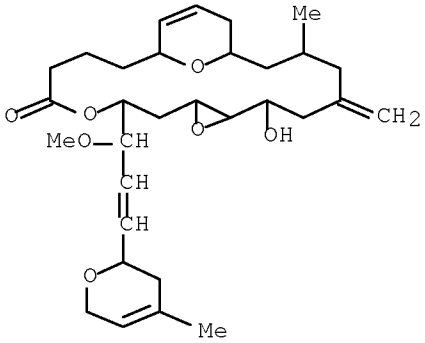

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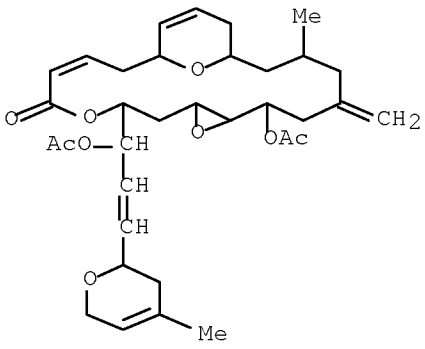

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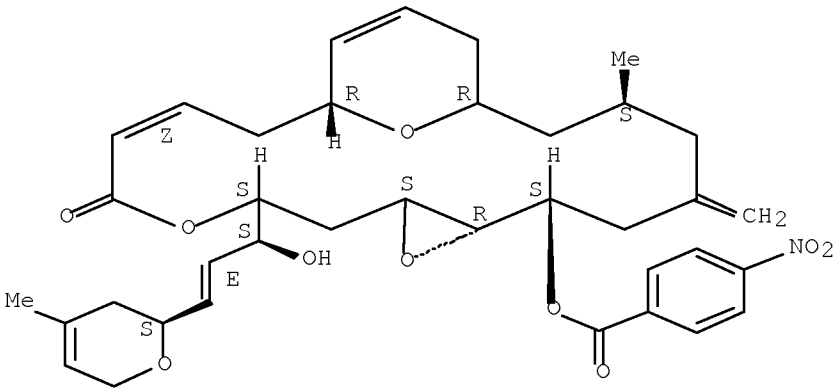
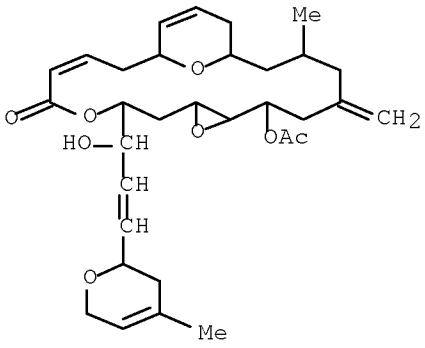
Absolute stereochemistry.
Double bond geometry as shown.

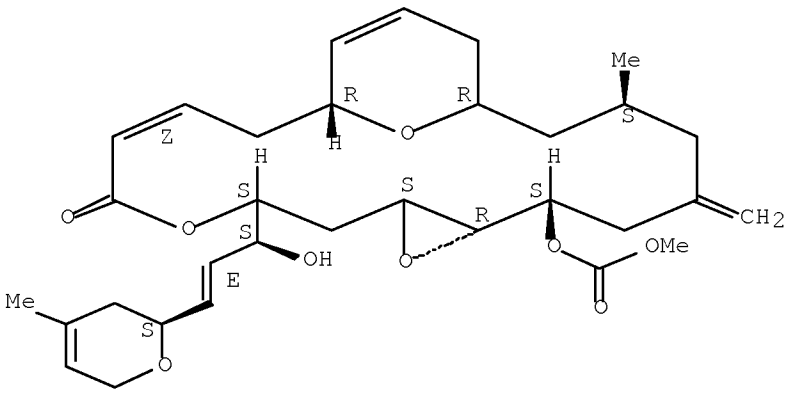


RN 676473-99-7 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-(acetyloxy)-12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



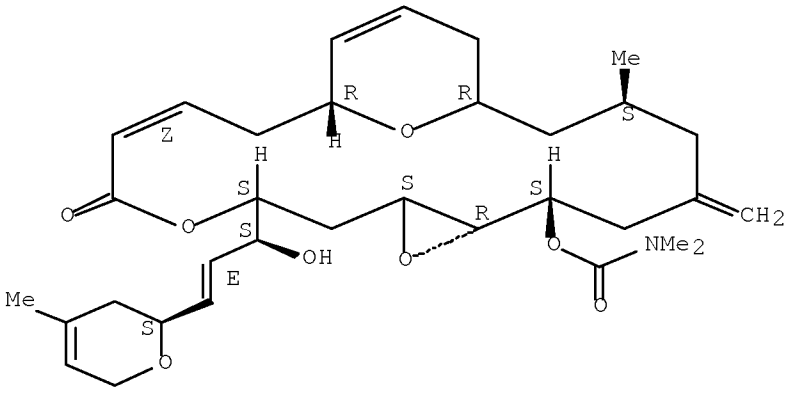
RN 676474-01-4 CAPLUS
CN Carbonic acid, (1R,3S,7S,8R,10S,12S,15Z,18R)-12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-3-methyl-5-methylene-14-oxo-9,13,22-trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-7-yl methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

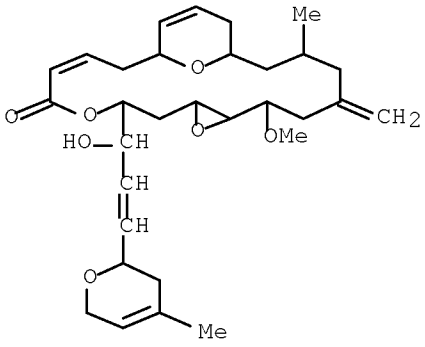


RN 676474-03-6 CAPLUS
CN Carbamic acid, dimethyl-, (1R,3S,7S,8R,10S,12S,15Z,18R)-12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-3-methyl-5-methylene-14-oxo-9,13,22-trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-7-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

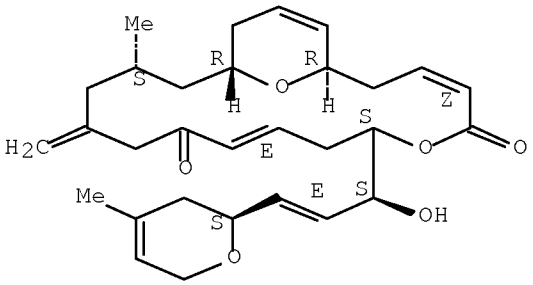


RN 676474-04-7 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-7-methoxy-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

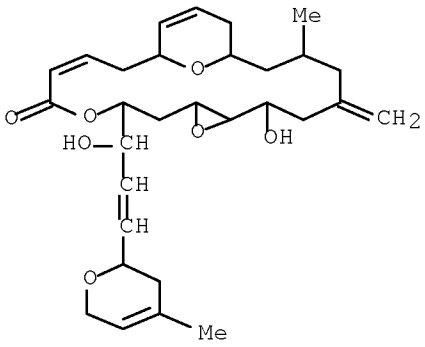


RN 676474-05-8 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-triene-5,11-dione, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-15-methyl-13-methylene-, (1R,3Z,7S,9E,15S,17R)- (9CI) (CA INDEX NAME)

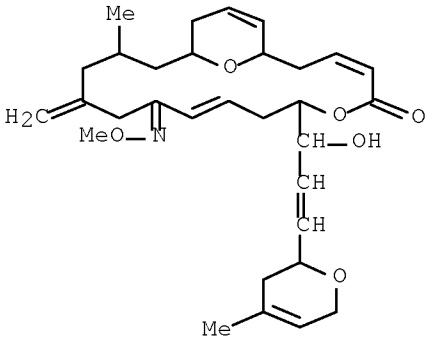
Absolute stereochemistry.
Double bond geometry as shown.



RN 676474-06-9 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7R,8R,10R,12S,15Z,18R)- (9CI) (CA INDEX NAME)

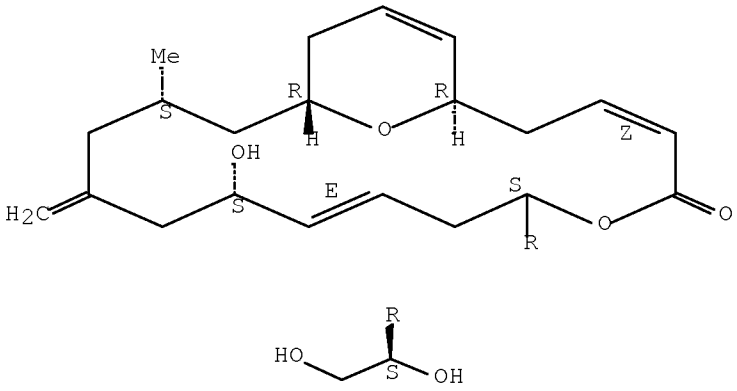


RN 676474-26-3 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-triene-5,11-dione, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-15-methyl-13-methylene-, 11-(O-methyloxime), (1R,3Z,7S,9E,15S,17R)- (9CI) (CA INDEX NAME)



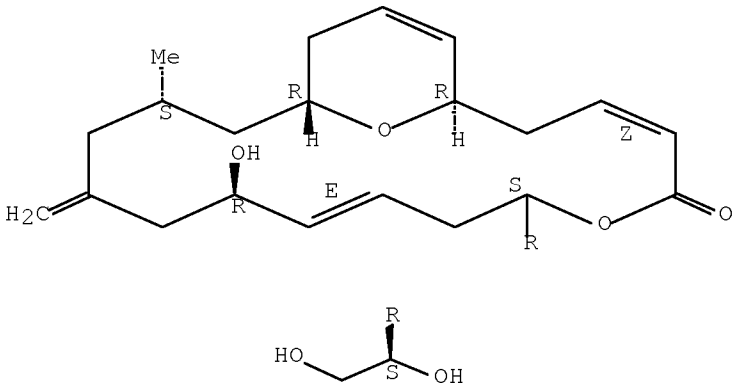
RN 849362-19-2 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S)-1,2-dihydroxyethyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



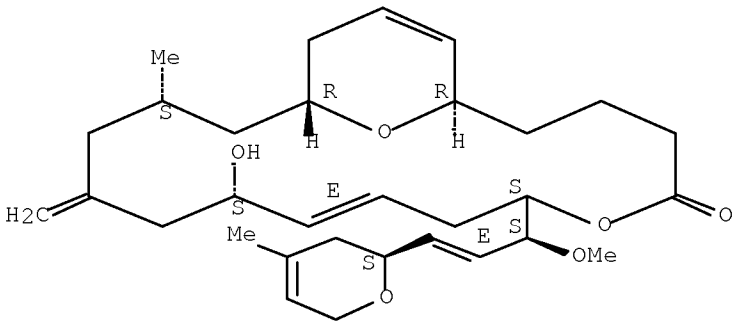
RN 849524-67-0 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S)-1,2-dihydroxyethyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11R,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



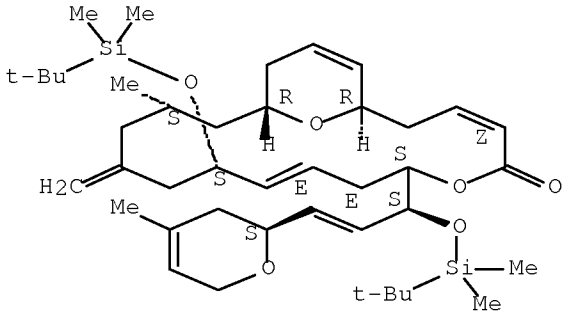
RN 849526-27-8 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-9,19-dien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,7S,9E,11S,15S,17R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



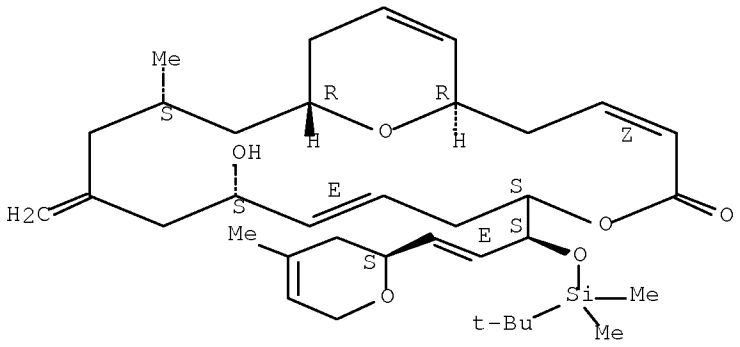
IT 449142-46-5P 676473-84-0P 849361-90-6P
849361-97-3P 849361-98-4P 849361-99-5P
849362-11-4P 849362-12-5P 849362-13-6P
849362-17-0P 849362-18-1P 849362-21-6P
849362-22-7P 849362-24-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of laulimalide analogs for use in pharmaceutical compns. as chemotherapeutic, antiproliferative, anticancer agents)
RN 449142-46-5 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



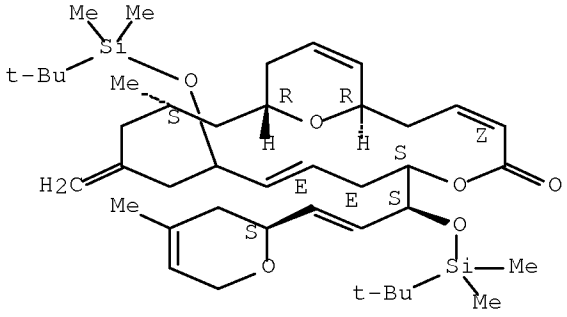
RN 676473-84-0 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



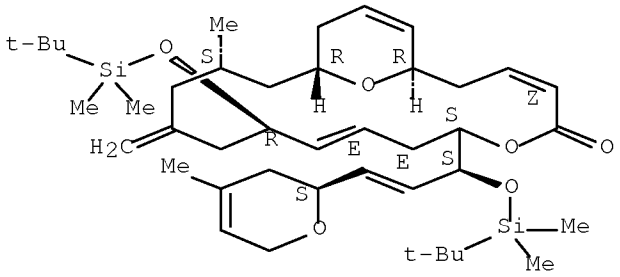
RN 849361-90-6 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-15-methyl-13-methylene-, (1R,3Z,7S,9E,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



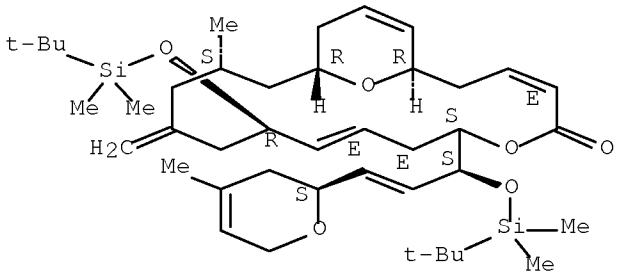
RN 849361-97-3 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-15-methyl-13-methylene-, (1R,3Z,7S,9E,11R,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



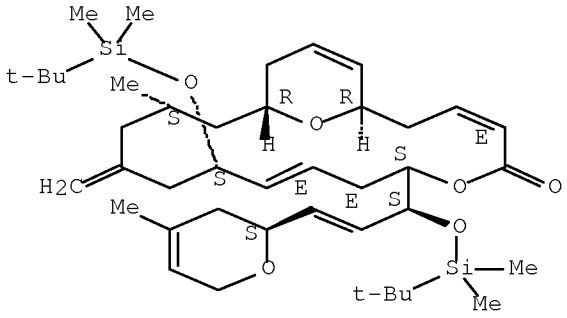
RN 849361-98-4 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-15-methyl-13-methylene-, (1R,3E,7S,9E,11R,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



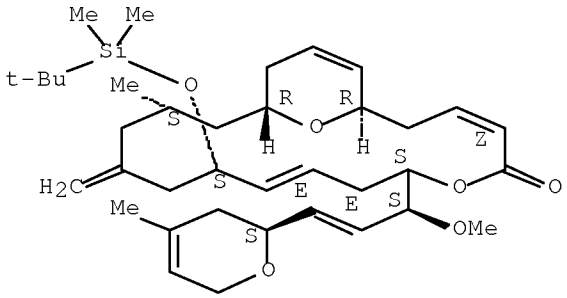
RN 849361-99-5 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-15-methyl-13-methylene-, (1R,3E,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 849362-11-4 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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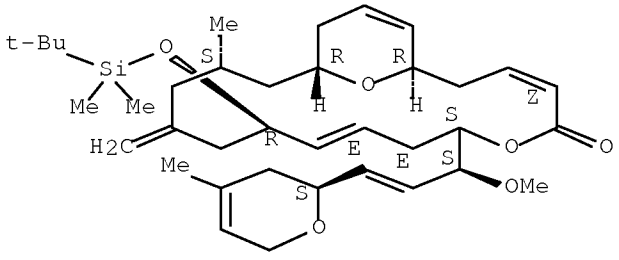
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-15-methyl-13-methylene-, (1R,3Z,7S,9E,11R,15S,17R)- (9CI) (CA INDEX NAME)

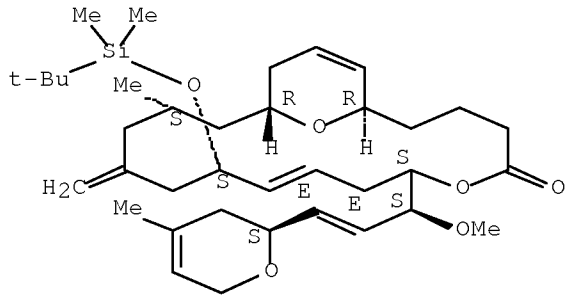
Absolute stereochemistry.
Double bond geometry as shown.



RN 849362-13-6 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-9,19-dien-5-one,

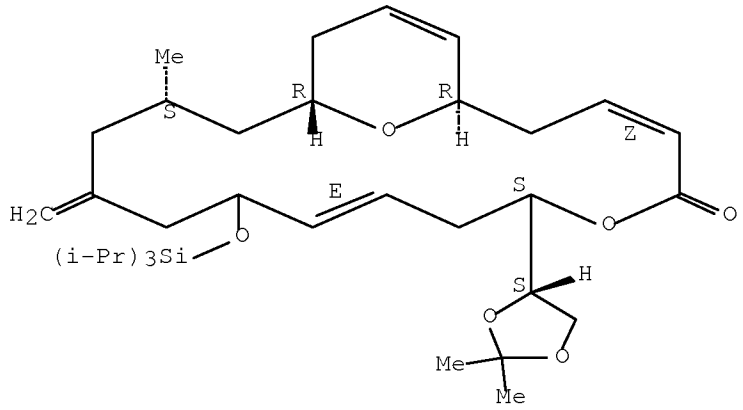
7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-15-methyl-13-methylene-, (1R,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



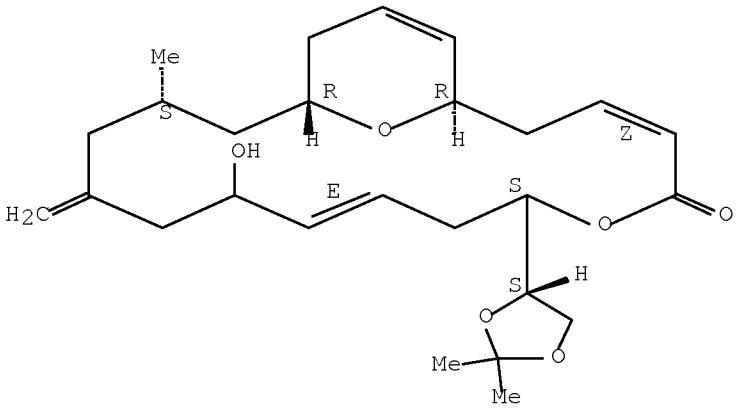
RN 849362-17-0 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(4S)-2,2-dimethyl-1,3-dioxolan-4-yl]-15-methyl-13-methylene-11-[[tris(1-methylethyl)silyl]oxy]-, (1R,3Z,7S,9E,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



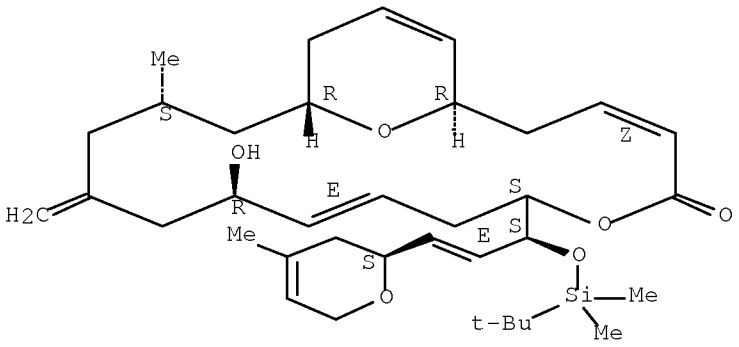
RN 849362-18-1 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(4S)-2,2-dimethyl-1,3-dioxolan-4-yl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



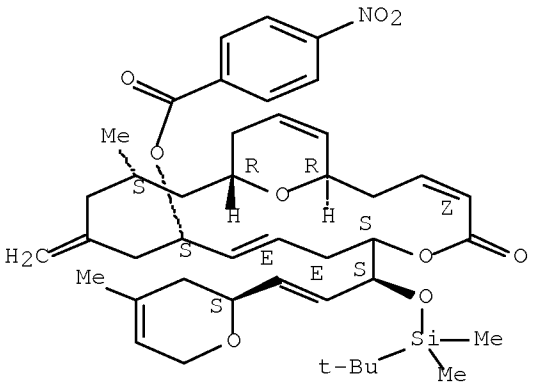
RN 849362-21-6 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11R,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



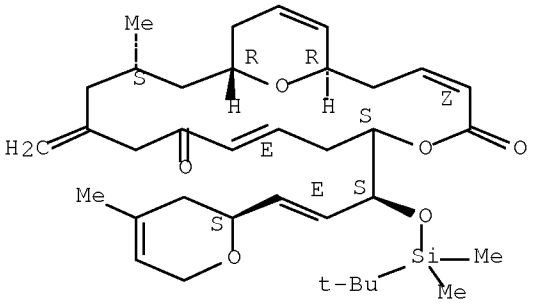
RN 849362-22-7 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-15-methyl-13-methylene-11-[(4-nitrobenzoyl)oxy]-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 849362-24-9 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-triene-5,11-dione, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-15-methyl-13-methylene-, (1R,3Z,7S,9E,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L26 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:44316 CAPLUS Full-text
DOCUMENT NUMBER: 142:297915
TITLE: Synthesis of 8-(S)-methoxy-11-desmethyl laulimalide: a novel laulimalide analogue
AUTHOR(S): Gallagher, Brian M.; Zhao, Hongjuan ; Pesant, Marc; Fang, Francis G.
CORPORATE SOURCE: Eisai Research Institute, Wilmington, MA, 01887, USA
SOURCE: Tetrahedron Letters (2005), 46(6), 923-926
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:297915
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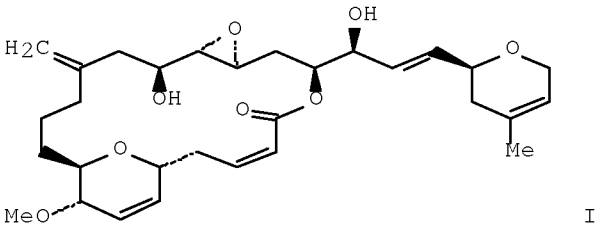


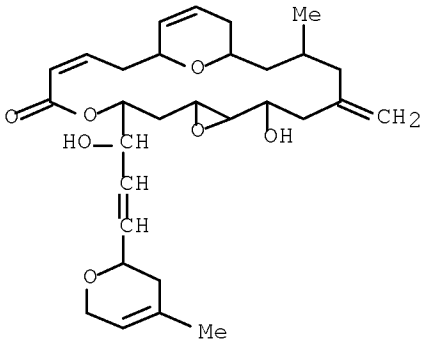
I

AB A strategy is outlined which enables preparation of novel laulimalide analogs at C.8 and C.11. A representative analog, 8-(S)-methoxy-11-desmethyl laulimalide (I), was synthesized via this route.

IT 115268-43-4DP, Laulimalide, analog
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation of 8-(S)-methoxy-11-desmethyl laulimalide)

RN 115268-43-4 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:51778 CAPLUS Full-text

DOCUMENT NUMBER: 140:303453

TITLE: Synthesis and biological evaluation of (-)-laulimalide analogues

AUTHOR(S): Gallagher, Brian M.; Fang, Francis G.; Johannes, Charles W.; Pesant, Marc; Tremblay, Martin R.; Zhao, Hongjuan ; Akasaka, Kozo; Li, Xiang-Yi; Liu, Junke; Littlefield, Bruce A.

CORPORATE SOURCE: Eisai Research Institute, Wilmington, MA, 01887, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(3), 575-579
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

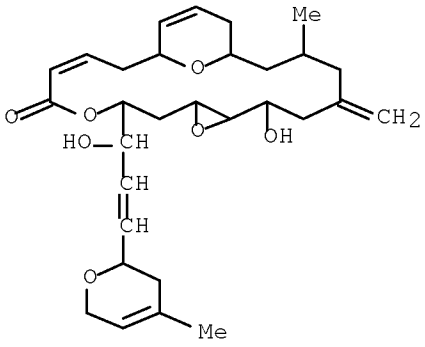
OTHER SOURCE(S): CASREACT 140:303453

AB Analogs of the marine natural product (-)-laulimalide were prepared by total synthesis and evaluated in vitro for anticancer activity.

IT 115268-43-4P, (-)-Laulimalide 352208-15-2P
352208-18-5P 352208-19-6P 385809-27-8P
676473-87-3P 676473-89-5P 676473-91-9P
676473-94-2P 676473-96-4P 676473-97-5P
676473-99-7P 676474-01-4P 676474-03-6P
676474-04-7P 676474-05-8P 676474-06-9P
676474-07-0P 676474-26-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor evaluation of (-)-laulimalide analogs derived from (S)-citronellal, and D-arabinose)

RN 115268-43-4 CAPLUS

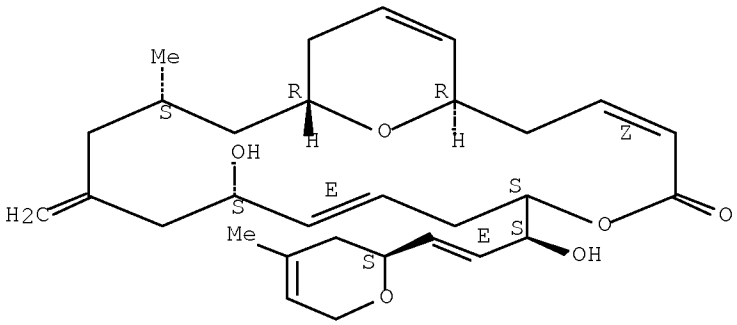
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



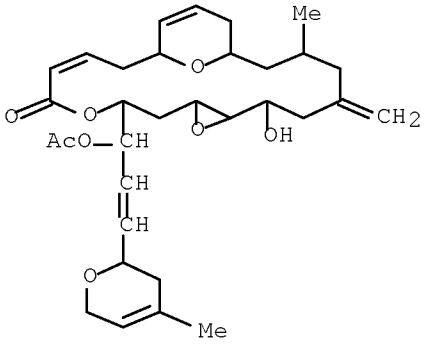
RN 352208-15-2 CAPLUS

CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

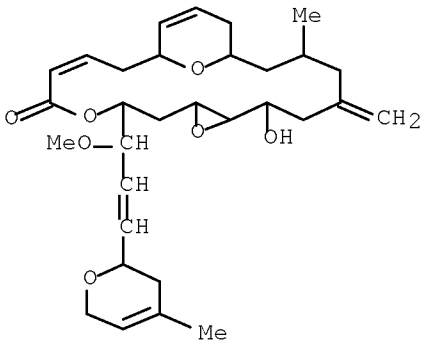
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 352208-18-5 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-1-(acetyloxy)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)-(9CI) (CA INDEX NAME)

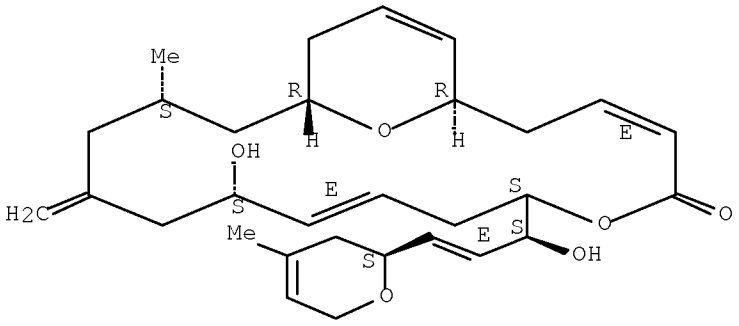


RN 352208-19-6 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)-(9CI) (CA INDEX NAME)



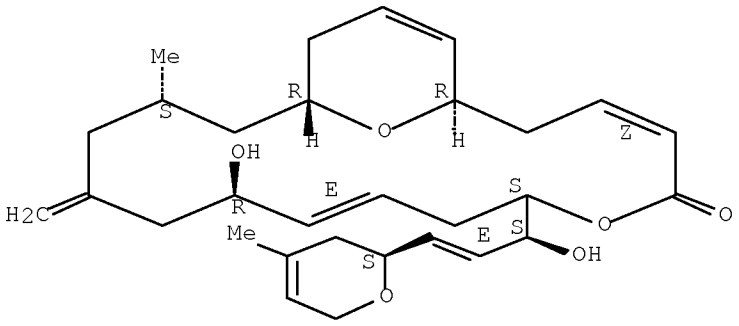
RN 385809-27-8 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3E,7S,9E,11S,15S,17R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



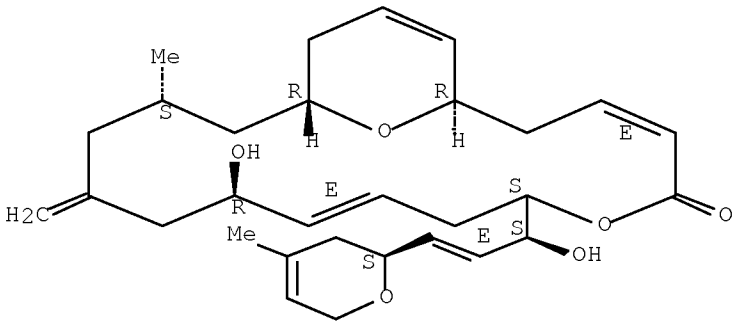
RN 676473-87-3 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11R,15S,17R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

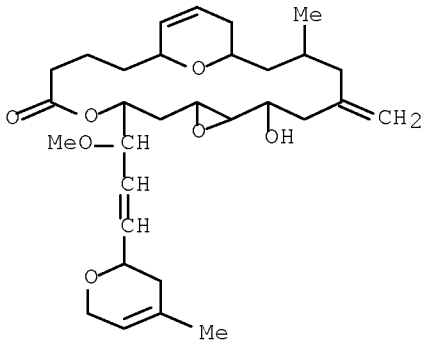


RN 676473-89-5 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3E,7S,9E,11R,15S,17R)-(9CI) (CA INDEX NAME)

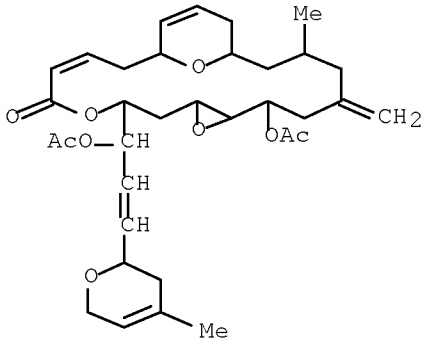
Absolute stereochemistry.
Double bond geometry as described by E or Z.



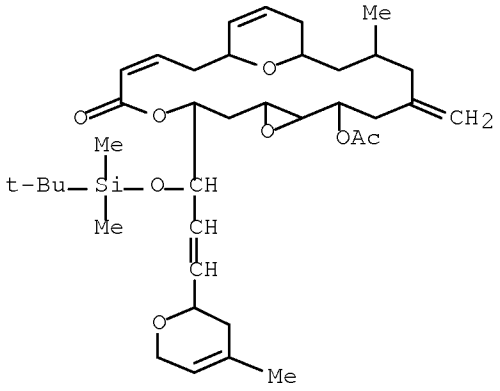
RN 676473-91-9 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docos-19-en-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,18R)- (9CI) (CA INDEX NAME)



RN 676473-94-2 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-(acetyloxy)-12-[(1S,2E)-1-(acetyloxy)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-2-propenyl]-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

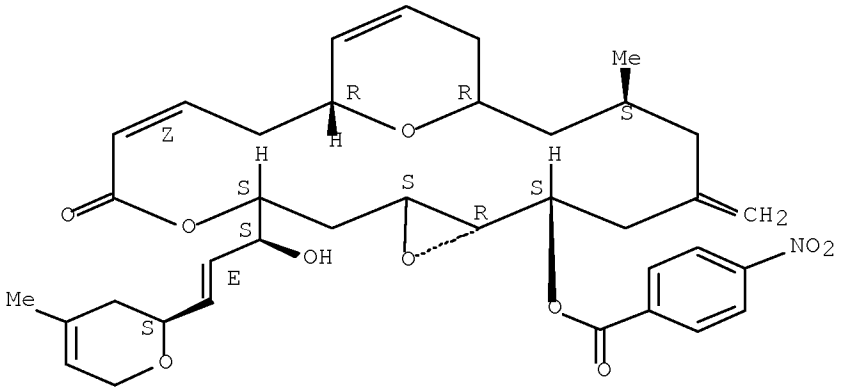


RN 676473-96-4 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-(acetyloxy)-12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

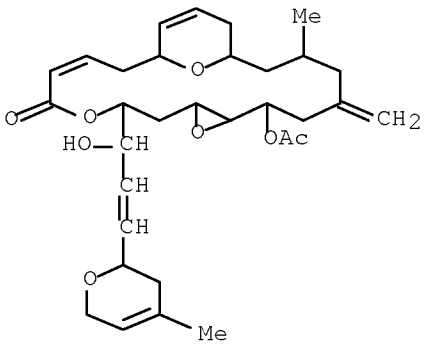


RN 676473-97-5 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-3-methyl-5-methylene-7-[(4-nitrobenzoyl)oxy]-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

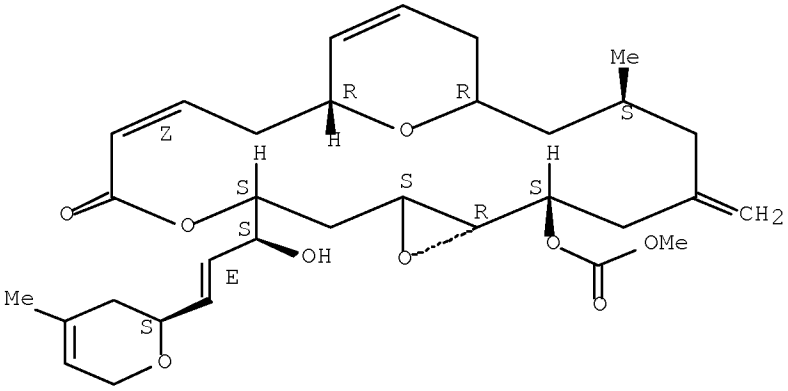


RN 676473-99-7 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-(acetyloxy)-12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



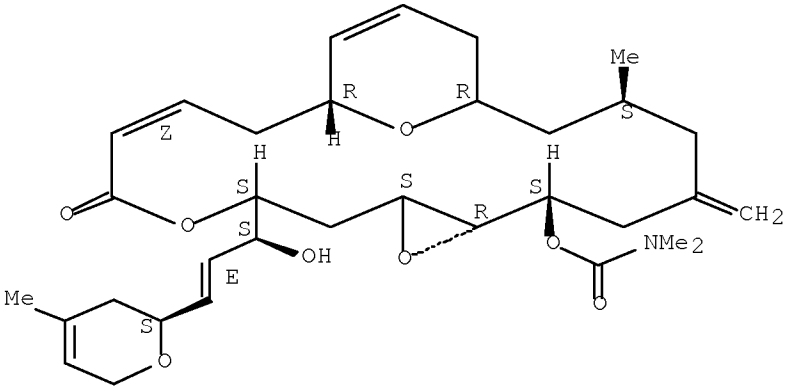
RN 676474-01-4 CAPLUS
CN Carbonic acid, (1R,3S,7S,8R,10S,12S,15Z,18R)-12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-3-methyl-5-methylene-14-oxo-9,13,22-trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-7-yl methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

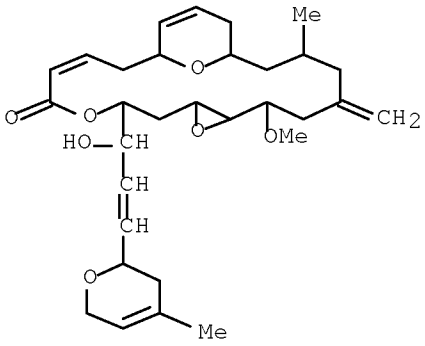


RN 676474-03-6 CAPLUS
CN Carbamic acid, dimethyl-, (1R,3S,7S,8R,10S,12S,15Z,18R)-12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-3-methyl-5-methylene-14-oxo-9,13,22-trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-7-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

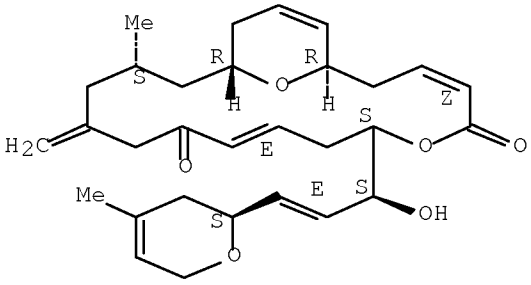


RN 676474-04-7 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-7-methoxy-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

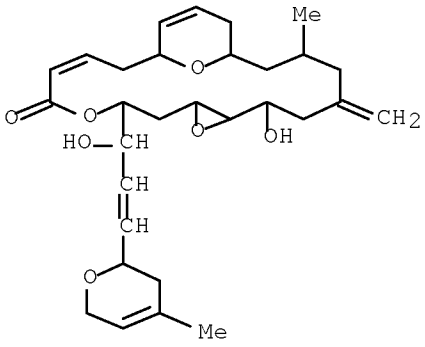


RN 676474-05-8 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-triene-5,11-dione, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-15-methyl-13-methylene-, (1R,3Z,7S,9E,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

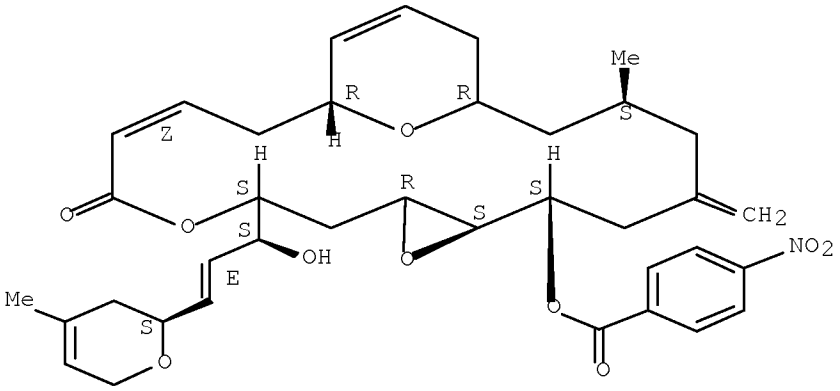


RN 676474-06-9 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7R,8R,10R,12S,15Z,18R)- (9CI) (CA INDEX NAME)



RN 676474-07-0 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-3-methyl-5-methylene-7-[(4-nitrobenzoyl)oxy]-, (1R,3S,7S,8S,10R,12S,15Z,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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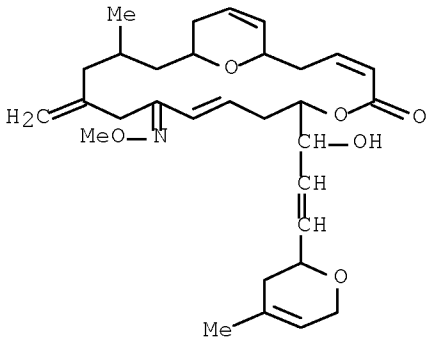
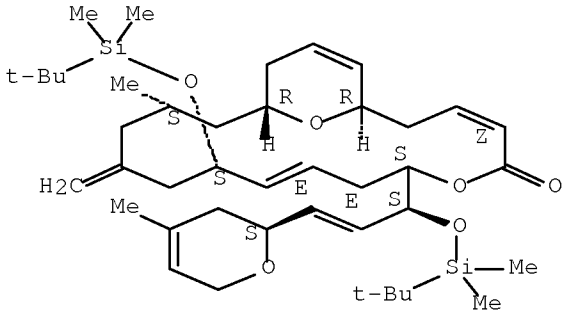
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-triene-5,11-dione, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-15-methyl-13-methylene-, 11-(O-methyloxime), (1R,3Z,7S,9E,15S,17R)- (9CI) (CA INDEX NAME)



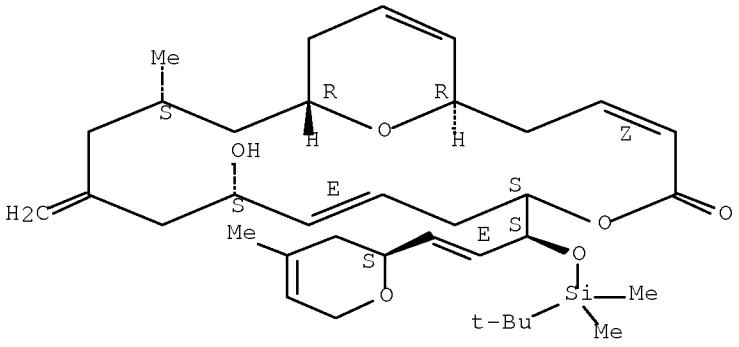
IT 449142-46-5P 676473-84-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor evaluation of (-)-laulimalide analogs derived from (S)-citronellal, and D-arabinose)
RN 449142-46-5 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 676473-84-0 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

STRUCTURE SEARCH PART 1

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=> fil reg; d stat que l10
FILE 'REGISTRY' ENTERED AT 09:20:08 ON 10 MAR 2009
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DICTIONARY FILE UPDATES:   8 MAR 2009  HIGHEST RN 1117698-24-4

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experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

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L1              STR
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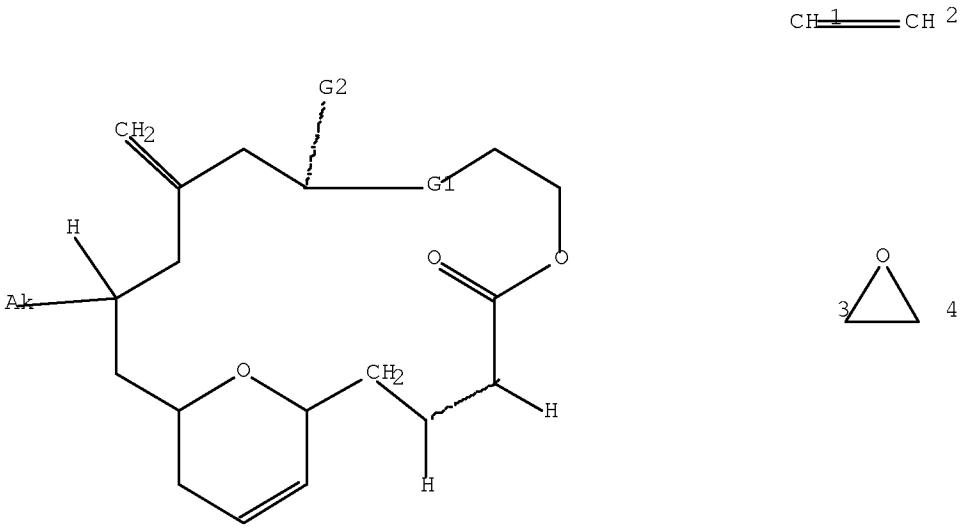
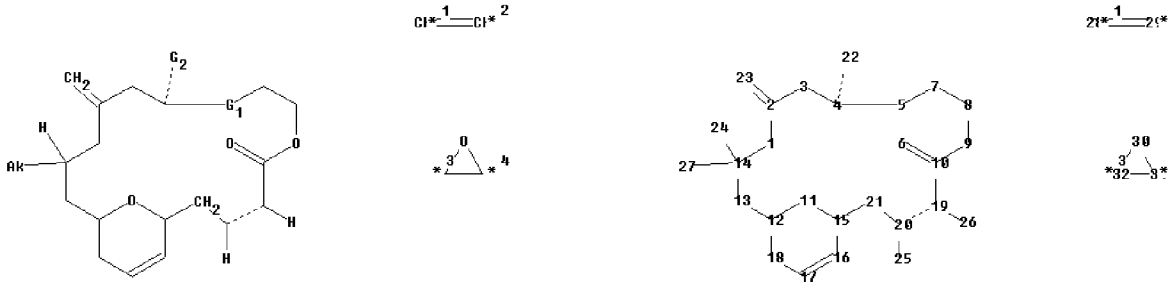


G1 [@1-@2],[@3-@4]
G2 O,N

Structure attributes must be viewed using STN Express query preparation.

Uploading L1.str



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6 22 23 24 25 26 27 28 29
ring nodes :
1 2 3 4 5 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 30 31 32
chain bonds :
2-23 4-22 6-10 14-24 14-27 19-26 20-25 28-29
ring bonds :
1-14 1-2 2-3 3-4 4-5 5-7 7-8 8-9 9-10 10-19 11-15 11-12 12-13 12-18
13-14 15-16 15-21 16-17 17-18 19-20 20-21 30-31 30-32 31-32
exact/norm bonds :
1-14 1-2 2-3 2-23 3-4 4-5 4-22 5-7 6-10 7-8 8-9 9-10 10-19 11-15 11-
12 12-13 12-18 13-14 14-24 14-27 15-16 15-21 16-17 17-18 19-20 19-26
20-21 20-25 28-29 30-31 30-32 31-32

G1:[*1-*2],[*3-*4]

G2:O,N

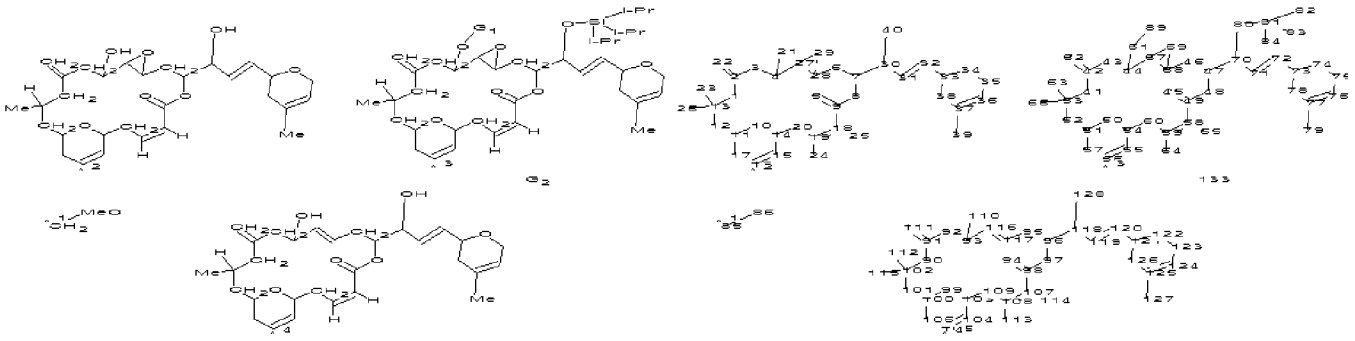
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS 29:CLASS 30:Atom 31:Atom 32:Atom

L2 119 SEA FILE=REGISTRY SSS FUL L1
L3 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

Uploading L3.str



chain nodes :
5 21 22 23 24 25 26 30 31 32 39 40 45 61 62 63 64 65 66 70 71
72 79 80 81 82 83 84 85 86 89 94 110 111 112 113 114 115 118 119
120 127 128 133
ring nodes :
1 2 3 4 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 27 28 29 33
34 35 36 37 38 41 42 43 44 46 47 48 49 50 51 52 53 54 55 56 57
58 59 60 67 68 69 73 74 75 76 77 78 90 91 92 93 95 96 97 98 99
100 101 102 103 104 105 106 107 108 109 116 117 121 122 123 124 125
126
chain bonds :
2-22 4-21 5-9 7-30 13-23 13-26 18-25 19-24 30-31 30-40 31-32 32-33 37-
39 42-62 44-61 45-49 47-70 53-63 53-66 58-65 59-64 61-89 70-71 70-80
71-72 72-73 77-79 80-81 81-82 81-83 81-84 85-86 91-111 93-110 94-98 96-
118 102-112 102-115 107-114 108-113 118-119 118-128 119-120 120-121 125-
127
ring bonds :
1-13 1-2 2-3 3-4 4-27 6-7 6-28 7-8 8-9 9-18 10-14 10-11 11-12 11-17
12-13 14-15 14-20 15-16 16-17 18-19 19-20 27-28 27-29 28-29 33-34 33-38
34-35 35-36 36-37 37-38 41-53 41-42 42-43 43-44 44-67 46-47 46-68 47-48
48-49 49-58 50-54 50-51 51-52 51-57 52-53 54-55 54-60 55-56 56-57 58-59
59-60 67-68 67-69 68-69 73-74 73-78 74-75 75-76 76-77 77-78 90-102 90-91
91-92 92-93 93-116 95-96 95-117 96-97 97-98 98-107 99-103 99-100 100-101
100-106 101-102 103-104 103-109 104-105 105-106 107-108 108-109 116-117
121-122 121-126 122-123 123-124 124-125 125-126
exact/norm bonds :
1-13 1-2 2-3 3-4 4-21 4-27 5-9 6-7 6-28 7-8 8-9 9-18 10-14 10-11 11-
12 11-17 12-13 14-15 14-20 15-16 16-17 18-19 19-20 27-28 27-29 28-29
30-40 33-34 33-38 34-35 35-36 36-37 37-38 41-53 41-42 42-43 43-44 44-61
44-67 45-49 46-47 46-68 47-48 48-49 49-58 50-54 50-51 51-52 51-57 52-53
54-55 54-60 55-56 56-57 58-59 59-60 61-89 67-68 67-69 68-69 70-80 73-74
73-78 74-75 75-76 76-77 77-78 90-102 90-91 91-92 92-93 93-110 93-116 94-
98 95-96 95-117 96-97 97-98 98-107 99-103 99-100 100-101 100-106 101-102
103-104 103-109 104-105 105-106 107-108 108-109 116-117 118-128 121-122
121-126 122-123 123-124 124-125 125-126
exact bonds :
2-22 7-30 13-23 13-26 18-25 19-24 30-31 31-32 32-33 37-39 42-62 47-70
53-63 53-66 58-65 59-64 70-71 71-72 72-73 77-79 80-81 81-82 81-83 81-84
85-86 91-111 96-118 102-112 102-115 107-114 108-113 118-119 119-120 120-
121 125-127

G1:H,[*1]

G2:[*2],[*3],[*4]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:CLASS 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom

11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:Atom
28:Atom 29:Atom 30:CLASS 31:CLASS 32:CLASS 33:Atom 34:CLASS 35:CLASS
36:CLASS 37:Atom 38:Atom 39:CLASS 40:CLASS 41:Atom 42:Atom 43:Atom 44:Atom
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79:CLASS 80:CLASS 81:CLASS 82:CLASS 83:CLASS 84:CLASS 85:CLASS 86:CLASS
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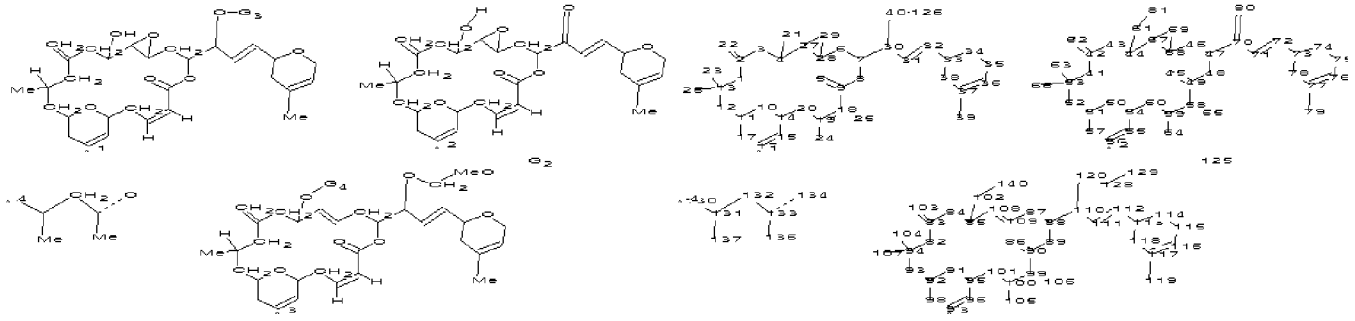
114:CLASS 115:CLASS 116:Atom 117:Atom 118:CLASS 119:CLASS 120:CLASS 121:Atom
122:CLASS 123:CLASS 124:CLASS 125:Atom 126:Atom 127:CLASS 128:CLASS
133:CLASS

L4 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

Uploading L4.str



chain nodes :
5 21 22 23 24 25 26 30 31 32 39 40 45 61 62 63 64 65 66 70 71
72 79 80 81 86 102 103 104 105 106 107 110 111 112 119 120 125 126
128 129 130 131 132 133 134 136 137 140
ring nodes :
1 2 3 4 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 27 28 29 33
34 35 36 37 38 41 42 43 44 46 47 48 49 50 51 52 53 54 55 56 57
58 59 60 67 68 69 73 74 75 76 77 78 82 83 84 85 87 88 89 90 91
92 93 94 95 96 97 98 99 100 101 108 109 113 114 115 116 117 118
chain bonds :
2-22 4-21 5-9 7-30 13-23 13-26 18-25 19-24 30-31 30-40 31-32 32-33 37-
39 40-126 42-62 44-61 45-49 47-70 53-63 53-66 58-65 59-64 61-81 70-71
70-80 71-72 72-73 77-79 83-103 85-102 86-90 88-110 94-104 94-107 99-106
100-105 102-140 110-111 110-120 111-112 112-113 117-119 120-128 128-129
130-131 131-132 131-137 132-133 133-134 133-136
ring bonds :
1-13 1-2 2-3 3-4 4-27 6-7 6-28 7-8 8-9 9-18 10-14 10-11 11-12 11-17
12-13 14-15 14-20 15-16 16-17 18-19 19-20 27-28 27-29 28-29 33-34 33-38
34-35 35-36 36-37 37-38 41-53 41-42 42-43 43-44 44-67 46-47 46-68 47-48
48-49 49-58 50-54 50-51 51-52 51-57 52-53 54-55 54-60 55-56 56-57 58-59
59-60 67-68 67-69 68-69 73-74 73-78 74-75 75-76 76-77 77-78 82-94 82-83
83-84 84-85 85-108 87-88 87-109 88-89 89-90 90-99 91-95 91-92 92-93 92-

98 93-94 95-96 95-101 96-97 97-98 99-100 100-101 108-109 113-114 113-118
114-115 115-116 116-117 117-118
exact/norm bonds :
1-13 1-2 2-3 3-4 4-21 4-27 5-9 6-7 6-28 7-8 8-9 9-18 10-14 10-11 11-
12 11-17 12-13 14-15 14-20 15-16 16-17 18-19 19-20 27-28 27-29 28-29
30-40 33-34 33-38 34-35 35-36 36-37 37-38 40-126 41-53 41-42 42-43 43-44
44-61 44-67 45-49 46-47 46-68 47-48 48-49 49-58 50-54 50-51 51-52 51-57
52-53 54-55 54-60 55-56 56-57 58-59 59-60 67-68 67-69 68-69 70-80 73-74
73-78 74-75 75-76 76-77 77-78 82-94 82-83 83-84 84-85 85-102 85-108 86-
90 87-88 87-109 88-89 89-90 90-99 91-95 91-92 92-93 92-98 93-94 95-96
95-101 96-97 97-98 99-100 100-101 102-140 108-109 110-120 113-114 113-118
114-115 115-116 116-117 117-118 133-134
exact bonds :
2-22 7-30 13-23 13-26 18-25 19-24 30-31 31-32 32-33 37-39 42-62 47-70
53-63 53-66 58-65 59-64 61-81 70-71 71-72 72-73 77-79 83-103 88-110 94-
104 94-107 99-106 100-105 110-111 111-112 112-113 117-119 120-128 128-129
130-131 131-132 131-137 132-133 133-136

G2:[*1],[*2],[*3]

G3:CH3,C(O)CH3

G4:H,[*4]

Connectivity :
134:1 E exact RC ring/chain
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:CLASS 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
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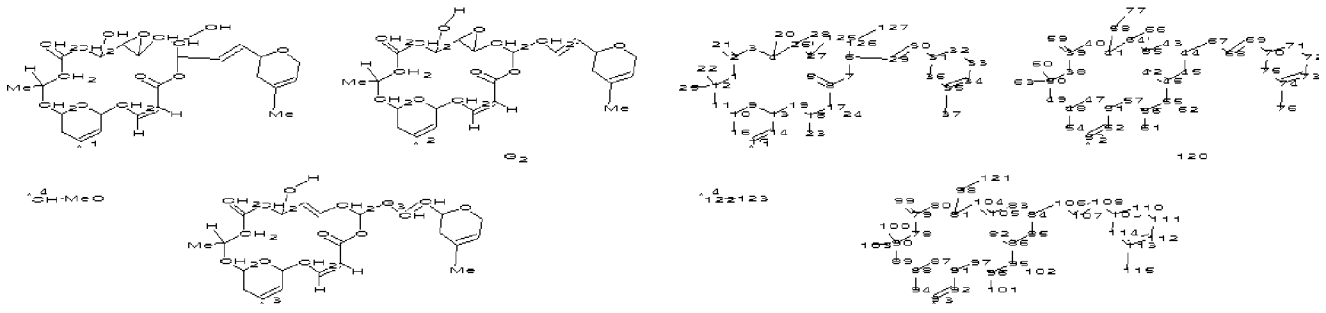
97:Atom 98:Atom 99:Atom 100:Atom 101:Atom 102:CLASS 103:CLASS 104:CLASS
105:CLASS 106:CLASS 107:CLASS 108:Atom 109:Atom 110:CLASS 111:CLASS
112:CLASS 113:Atom 114:CLASS 115:CLASS 116:CLASS 117:Atom 118:Atom 119:CLASS
120:CLASS 125:CLASS 126:CLASS 128:CLASS 129:CLASS 130:CLASS 131:CLASS
132:CLASS 133:CLASS 134:CLASS 136:CLASS 137:CLASS 140:CLASS

L5 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

Uploading L5.str



chain nodes :
5 20 21 22 23 24 25 29 30 37 42 58 59 60 61 62 63 67 68 69 76
77 82 98 99 100 101 102 103 106 107 108 115 120 121 122 123 127
ring nodes :
1 2 3 4 6 7 8 9 10 11 12 13 14 15 16 17 18 19 26 27 28 31 32
33 34 35 36 38 39 40 41 43 44 45 46 47 48 49 50 51 52 53 54 55
56 57 64 65 66 70 71 72 73 74 75 78 79 80 81 83 84 85 86 87 88
89 90 91 92 93 94 95 96 97 104 105 109 110 111 112 113 114 125
126
chain bonds :
2-21 4-20 5-8 6-29 12-22 12-25 17-24 18-23 29-30 30-31 35-37 39-59 41-
58 42-46 44-67 50-60 50-63 55-62 56-61 58-77 67-68 68-69 69-70 74-76
79-99 81-98 82-86 84-106 90-100 90-103 95-102 96-101 98-121 106-107 107-
108 108-109 113-115 122-123 126-127
ring bonds :
1-12 1-2 2-3 3-4 4-26 6-7 6-126 7-8 8-17 9-13 9-10 10-11 10-16 11-12
13-14 13-19 14-15 15-16 17-18 18-19 26-27 26-28 27-28 27-125 31-32 31-36
32-33 33-34 34-35 35-36 38-50 38-39 39-40 40-41 41-64 43-44 43-65 44-45
45-46 46-55 47-51 47-48 48-49 48-54 49-50 51-52 51-57 52-53 53-54 55-56
56-57 64-65 64-66 65-66 70-71 70-75 71-72 72-73 73-74 74-75 78-90 78-79
79-80 80-81 81-104 83-84 83-105 84-85 85-86 86-95 87-91 87-88 88-89 88-
94 89-90 91-92 91-97 92-93 93-94 95-96 96-97 104-105 109-110 109-114
110-111 111-112 112-113 113-114 125-126
exact/norm bonds :
1-12 1-2 2-3 3-4 4-20 4-26 5-8 6-7 6-126 7-8 8-17 9-13 9-10 10-11 10-
16 11-12 13-14 13-19 14-15 15-16 17-18 18-19 26-27 26-28 27-28 27-125
31-32 31-36 32-33 33-34 34-35 35-36 38-50 38-39 39-40 40-41 41-58 41-64
42-46 43-44 43-65 44-45 45-46 46-55 47-51 47-48 48-49 48-54 49-50 51-52
51-57 52-53 53-54 55-56 56-57 64-65 64-66 65-66 70-71 70-75 71-72 72-73
73-74 74-75 78-90 78-79 79-80 80-81 81-98 81-104 82-86 83-84 83-105 84-
85 84-106 85-86 86-95 87-91 87-88 88-89 88-94 89-90 91-92 91-97 92-93
93-94 95-96 96-97 104-105 106-107 109-110 109-114 110-111 111-112 112-113
113-114 125-126 126-127
exact bonds :
2-21 6-29 12-22 12-25 17-24 18-23 29-30 30-31 35-37 39-59 44-67 50-60
50-63 55-62 56-61 58-77 67-68 68-69 69-70 74-76 79-99 90-100 90-103 95-
102 96-101 98-121 107-108 108-109 113-115 122-123

G2:[*1],[*2],[*3]

G3:CH2,[*4]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:CLASS 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:Atom 27:Atom
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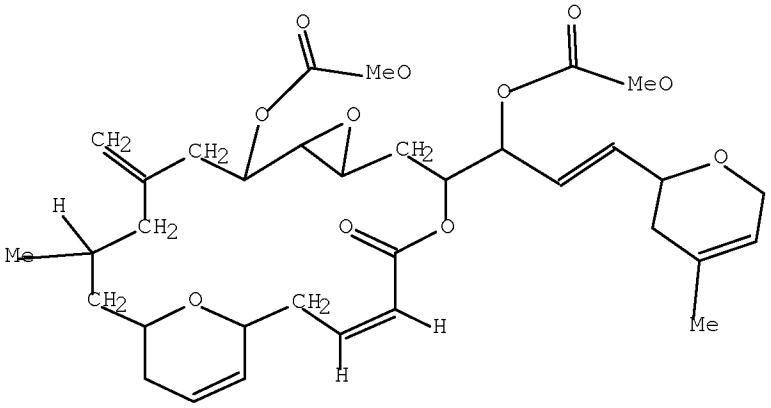
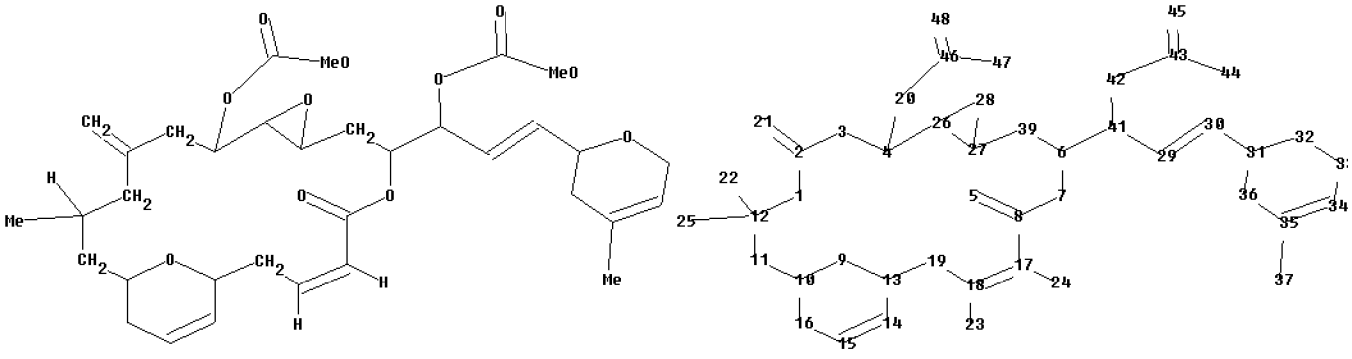
L6 STR



G1
G2
G3 CH2

Structure attributes must be viewed using STN Express query preparation.

Uploading L6.str



chain nodes :
5 20 21 22 23 24 25 29 30 37 41 42 43 44 45 46 47 48
ring nodes :
1 2 3 4 6 7 8 9 10 11 12 13 14 15 16 17 18 19 26 27 28 31 32
33 34 35 36 39
chain bonds :

2-21 4-20 5-8 6-41 12-22 12-25 17-24 18-23 20-46 29-30 29-41 30-31 35-37 41-42 42-43 43-44 43-45 46-47 46-48
ring bonds :
1-12 1-2 2-3 3-4 4-26 6-39 6-7 7-8 8-17 9-13 9-10 10-11 10-16 11-12 13-14 13-19 14-15 15-16 17-18 18-19 26-27 26-28 27-28 27-39 31-32 31-36 32-33 33-34 34-35 35-36
exact/norm bonds :
1-12 1-2 2-3 3-4 4-20 4-26 5-8 6-39 6-7 7-8 8-17 9-13 9-10 10-11 10-16 11-12 13-14 13-19 14-15 15-16 17-18 18-19 20-46 26-27 26-28 27-28 27-39 31-32 31-36 32-33 33-34 34-35 35-36 41-42 42-43 43-45 46-48
exact bonds :
2-21 6-41 12-22 12-25 17-24 18-23 29-30 29-41 30-31 35-37 43-44 46-47

G2

G3:CH2

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:CLASS 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:Atom 27:Atom 28:Atom 29:CLASS 30:CLASS 31:Atom 32:CLASS 33:CLASS 34:CLASS 35:Atom 36:Atom 37:CLASS 39:Atom 41:CLASS 42:CLASS 43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS

L9 21 SEA FILE=REGISTRY SUB=L2 SSS FUL (L3 OR L4 OR L5 OR L6)
L10 98 SEA FILE=REGISTRY SPE=ON ABB=ON L2 NOT L9

=> fil capl; d que nos l17
FILE 'CAPLUS' ENTERED AT 09:20:25 ON 10 MAR 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 10 Mar 2009 VOL 150 ISS 11
FILE LAST UPDATED: 9 Mar 2009 (20090309/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

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This file contains CAS Registry Numbers for easy and accurate
substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L1              STR
L2          119 SEA FILE=REGISTRY SSS FUL L1
L3              STR
L4              STR
L5              STR
L6              STR
L9           21 SEA FILE=REGISTRY SUB=L2 SSS FUL (L3 OR L4 OR L5 OR L6)
L10          98 SEA FILE=REGISTRY SPE=ON  ABB=ON  L2 NOT L9
L17          26 SEA FILE=CAPLUS SPE=ON  ABB=ON  L10


=> s l17 not l26
L40          24 L17 NOT L26    L26=INVENTOR SEARCH ANSWER SET

=> d ibib abs hitstr l40 1-24

L40  ANSWER 1 OF 24  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2009:197062  CAPLUS  Full-text
TITLE:                    Preparation of laulimalide analogues for the treatment
                          of abnormal cell proliferation
INVENTOR(S):              Wender, Paul A.
PATENT ASSIGNEE(S):       The Board of Trustees of the Leland Stanford Junior
                          University, USA
SOURCE:                   PCT Int. Appl., 232pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2009023123         A1    20090219    WO 2008-US9492          20080807
         W:  AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
             CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,
             FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
             KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
             ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
             PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ,
             TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
             IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
             TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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                                             US 2007-983992P     P  20071031
GI
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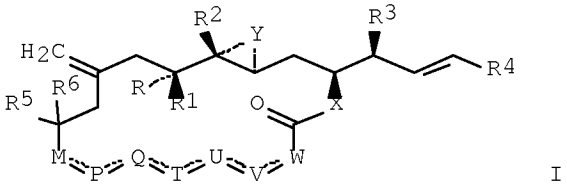

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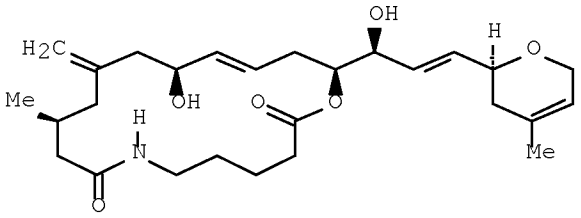
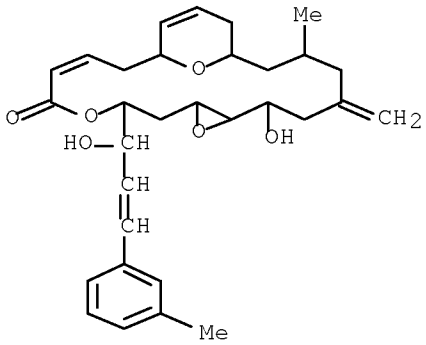


II

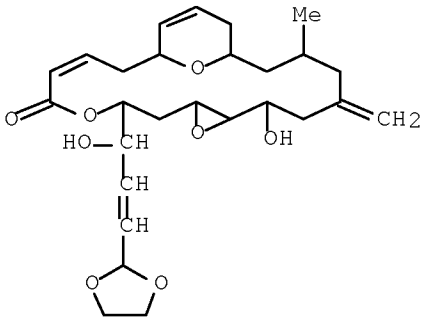
AB Laulimalide analogs of formula I [R, R1, R5, R6 = H, alkyl, alkoxy, aryl, etc.; R2 = absent, H, alkyl, alkoxy, aryl, etc.; R3 = H, OH, alkyl, alkoxy, aryl, etc.; R4 = heteroalkyl, cycloalkyl, (hetero)aryl, etc.; Y = bond, H, O, CH2, absent, etc.; X = O, CH2, S, NH, etc.; M, P, Q, T, U, V, W = (substituted) CH2, CH, CO, NH, O, alkylene, etc.] are prepared, which are useful as microtubule stabilizing agents and in the treatment of abnormal cell proliferation. Methods of making the compds., as well as methods of using such compds. in treating abnormal cell proliferation diseases are also described. Thus, II was prepared in several steps.

IT 1049737-12-3P 1049737-14-5P 1049737-16-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of laulimalide analogs for treatment of abnormal cell proliferation)

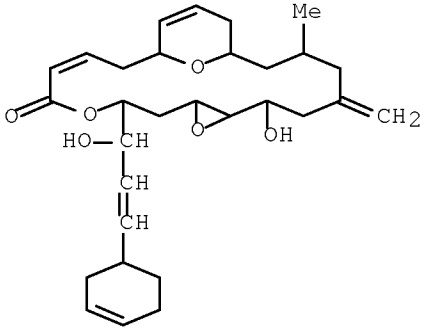
RN 1049737-12-3 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-16-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-3-(3-methylphenyl)-2-propen-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



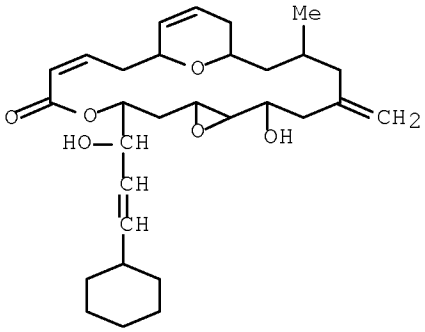
RN 1049737-14-5 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(1,3-dioxolan-2-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 1049737-16-7 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(3-cyclohexen-1-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



IT 911834-92-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of laulimalide analogs for treatment of abnormal cell proliferation)
RN 911834-92-9 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-cyclohexyl-1-hydroxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1122546 CAPLUS Full-text
DOCUMENT NUMBER: 149:378446
TITLE: Processes for the synthesis of laulimalide and its analogs and methods for the treatment of proliferative disease
INVENTOR(S): Wender, Paul
PATENT ASSIGNEE(S): The Board of Trustees of the Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 96pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2008112799	A1	20080918	WO 2008-US56710		20080312
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
US 20080227851	A1	20080918	US 2008-46632		20080312
PRIORITY APPLN. INFO.:			US 2007-906625P	P	20070312
			US 2007-983992P	P	20071031

OTHER SOURCE(S): MARPAT 149:378446
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

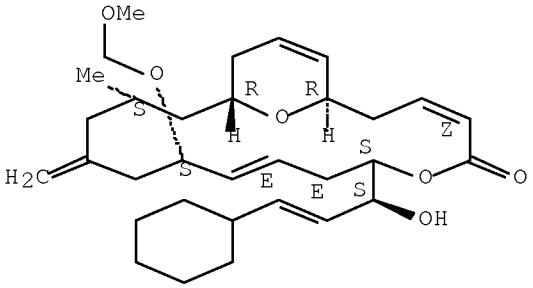
AB Novel laulimalide analogs I [R = 3,6-dihydro-4,5-dimethyl-2H-pyran-2-yl, 3,6-dihydro-2H-pyran-2-yl, 5,6-dihydro-2H-pyran-2-yl, 4-methyltetrahydro-2H-pyran-2-yl, 4,4-dimethyltetrahydro-2H-pyran-2-yl, 2-methyl-1-cyclohexen-4-yl, 1,2-dimethyl-1-cyclohexen-4-yl, 1-cyclohexen-4-yl, 1-methyl-1-cyclohexen-3-yl, 3-methylcyclohexyl, 3,3-dimethylcyclohexyl, 1,2,3,4-tetrahydronapnth-2-yl, 1-cyclohexen-3-yl, 1-cyclopenten-4-yl, 1-cyclohepten-3-yl, 1-cyclohepten-4-yl,CH2OMe, cyclohexyl, m-tolyl, 3,4-dihydro-4-oxopyran-2-yl, 1,3-dioxolan-2-yl, tetrahydropyran-2-yl, 1H-3,4-dihydroisobenzopyran-3-yl; R1 = H, Me; R2 = H, Me, Ac; X1, X2 = O, NH, NMe] or their pharmaceutically acceptable salts or solvates, methods for the treatment of proliferative disease and processes for the synthesis of laulimalide and novel laulimalide analogs are described. A process for the synthesis of I comprises: (a) placing macrolide II [R3 = H, Me, Et, CH2Et, Bu, CH2Bu, cyclohexyl, CHMe2, CH2OMe] in a reactor; (b) doing a cross-metathesis with a reactive alkene, RCH:CH2, in the presence of a

ruthenium catalyst. Thus, cyclohexenyl analog I (R = 1-cyclohexen-4-yl, R1 = Me, R2 = H, X1 = X2 = O) was prepared from macrolide III via cross-coupling with vinylcyclohexane in the presence of Grubb's second generation ruthenium catalyst, partial hydrogenation with H2 over Lindlar catalyst and quinoline, O-deprotection with BrBMe2 in CH2Cl2/(CH2Cl)2, stereoselective epoxidn. with Me3CO2H in the presence of Ti(OCHMe2)4 and diisopropyl (+)-tartrate in CH2Cl2, and a second cross-metathesis with 4-vinylcyclohexene. The antiproliferative activity of I (R = 1-cyclohexen-4-yl, R1 = Me, R2 = H, X1 = X2 = O) was determined [IC50 = 368 nM vs. human breast cancer carcinoma (MDA-MB-435)].

IT 911834-96-3P 1058706-83-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and O-dealkylation of; preparation of laulimalide and its analogs
for use in the treatment of proliferative diseases)

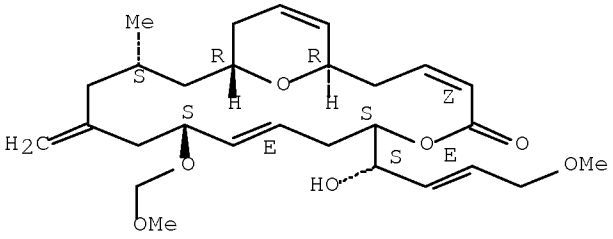
RN 911834-96-3 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-cyclohexyl-1-hydroxy-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 1058706-83-4 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-1-hydroxy-4-methoxy-2-buten-1-yl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,11S,13E,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

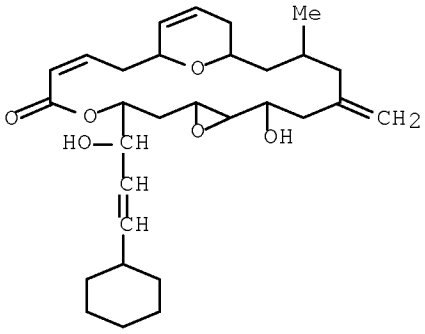


IT 911834-92-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and cross-metathesis of, with reactive alkenes; preparation of

laulimalide and its analogs for use in the treatment of proliferative diseases)

RN 911834-92-9 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-cyclohexyl-1-hydroxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



IT 1049737-05-4P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation and epoxidn. or cross-metathesis of, with vinylcyclohexane; preparation of laulimalide and its analogs for use in the treatment of proliferative diseases)

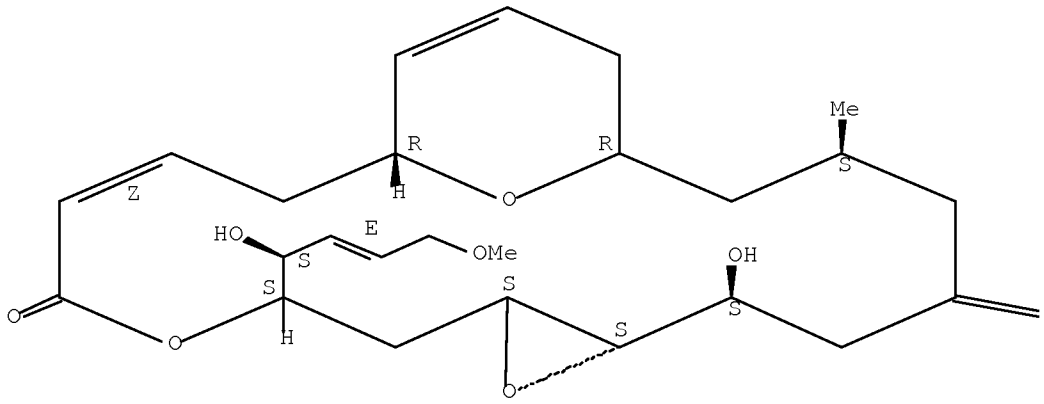
RN 1049737-05-4 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-4-methoxy-2-buten-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

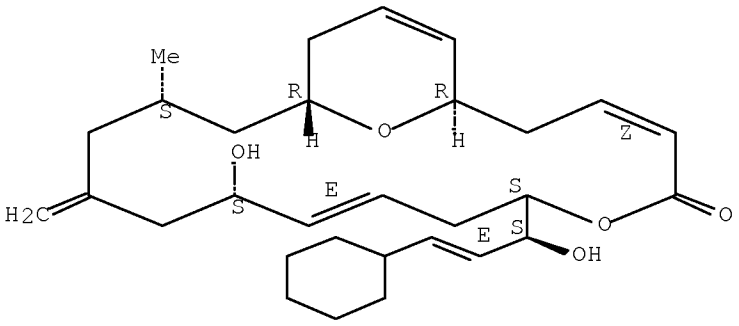
PAGE 1-A



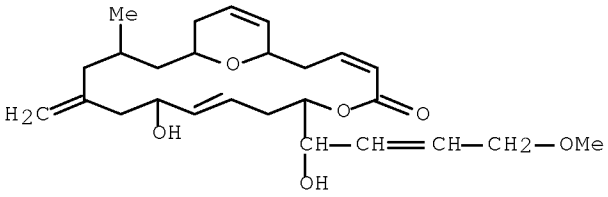
$=CH_2$

IT 911834-91-8P 1058706-84-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and regioselective, stereoselective epoxidn. of; preparation of
laulimalide and its analogs for use in the treatment of proliferative diseases)
RN 911834-91-8 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-cyclohexyl-1-hydroxy-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 1058706-84-5 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 11-hydroxy-7-[(1S,2E)-1-hydroxy-4-methoxy-2-buten-1-yl]-15-methyl-13-methylene-, (1R,3Z,7S,11S,13E,15S,17R)- (CA INDEX NAME)



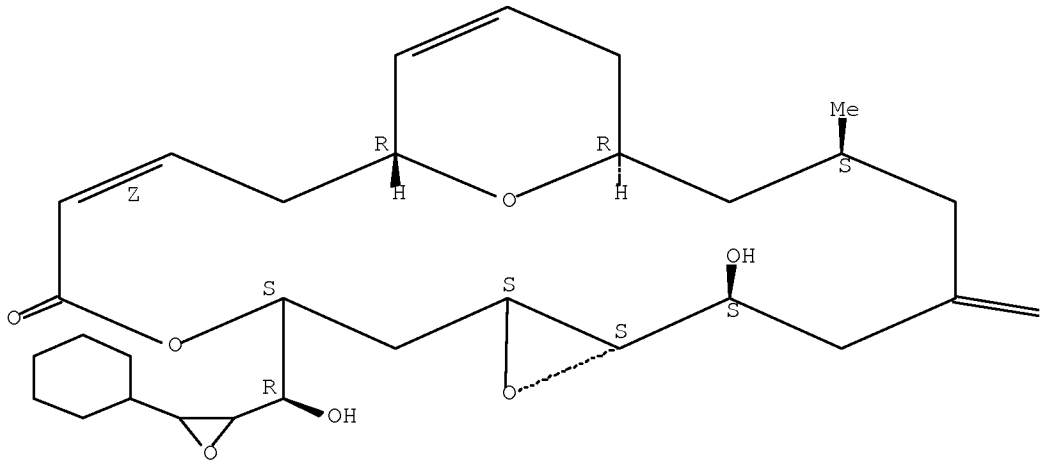
IT 1049737-10-1P 1049737-12-3P 1049737-14-5P
1049737-16-7P 1058707-42-8P 1058707-51-9P
1058707-55-3P 1058707-56-4P 1058707-57-5P
1058707-58-6P 1058707-59-7P 1058707-60-0P
1058707-61-1P 1058707-62-2P 1058707-64-4P
1058707-66-6P 1058707-68-8P 1058707-71-3P
1058707-75-7P 1058707-76-8P 1058707-77-9P
1058707-78-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of laulimalide and its analogs for use in the treatment of proliferative diseases)

RN 1049737-10-1 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(R)-(3-cyclohexyl-2-oxiranyl)hydroxymethyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

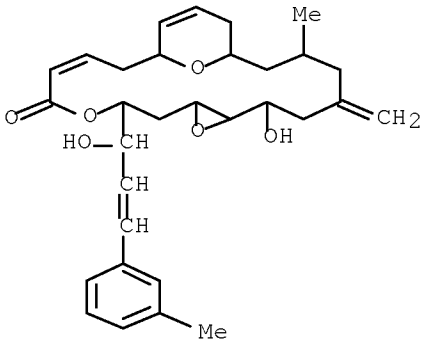
PAGE 1-A



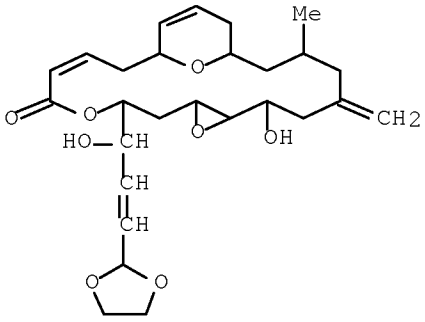
PAGE 1-B

$=CH_2$

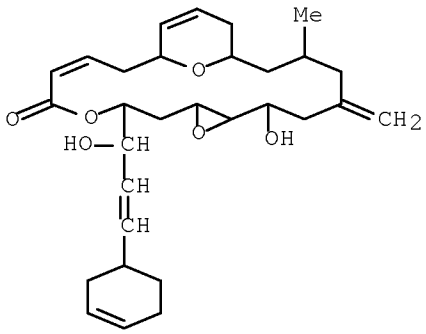
RN 1049737-12-3 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-16-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-3-(3-methylphenyl)-2-propen-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



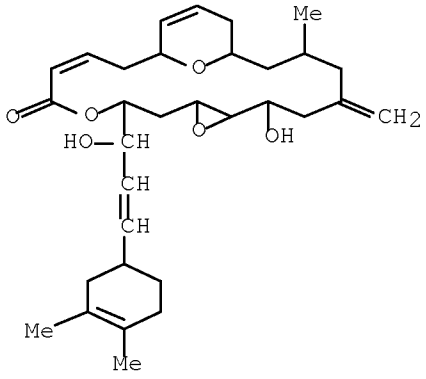
RN 1049737-14-5 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(1,3-dioxolan-2-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



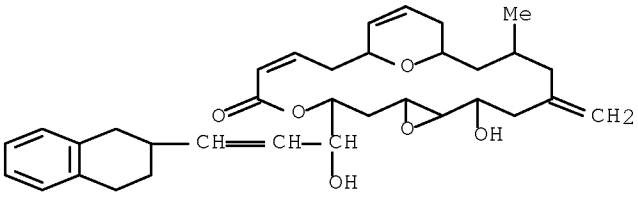
RN 1049737-16-7 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(3-cyclohexen-1-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 1058707-42-8 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(3,4-dimethyl-3-cyclohexen-1-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 1058707-51-9 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-3-(1,2,3,4-tetrahydro-2-naphthalenyl)-2-propen-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 1058707-55-3 CAPLUS
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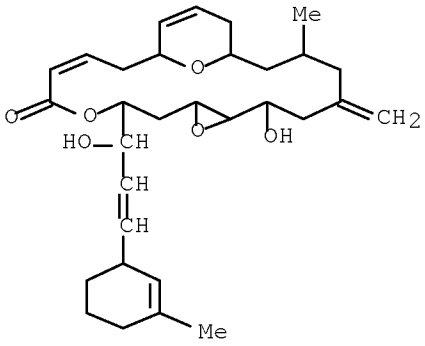
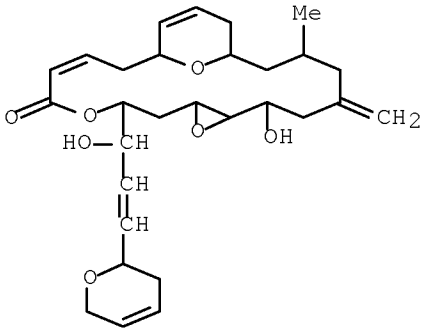
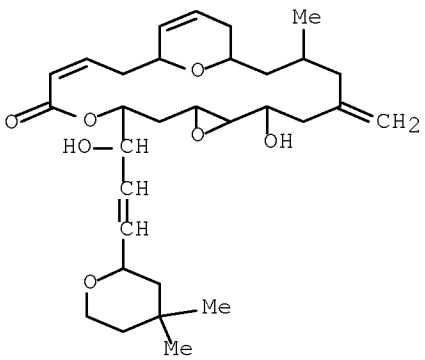


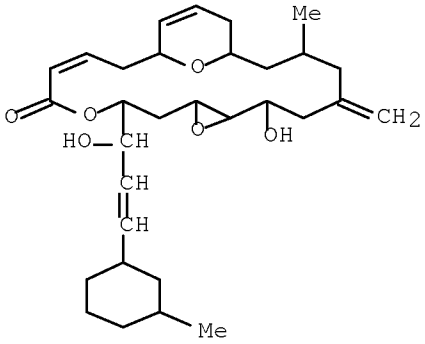
RN 1058707-56-4 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(3,6-dihydro-2H-pyran-2-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 1058707-57-5 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-3-(tetrahydro-4,4-dimethyl-2H-pyran-2-yl)-2-propen-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 1058707-58-6 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-3-(3-methylcyclohexyl)-2-propen-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



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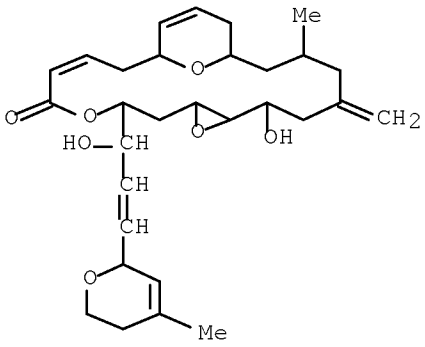
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(5,6-dihydro-4-methyl-2H-pyran-2-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



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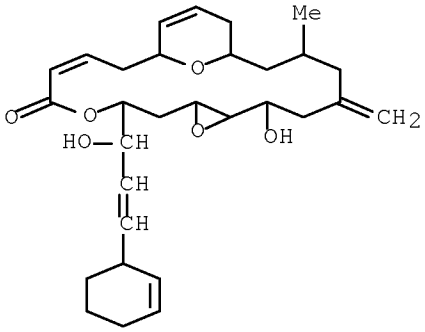
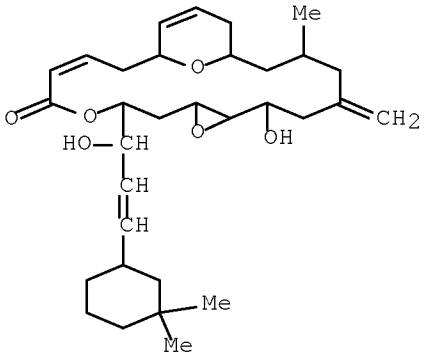
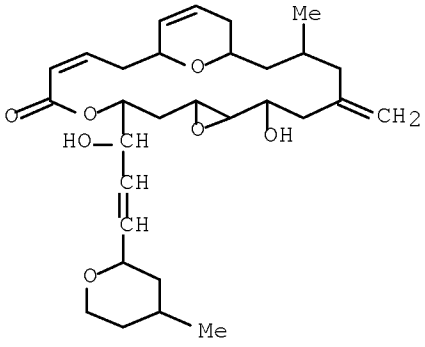


RN 1058707-61-1 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(3,3-dimethylcyclohexyl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

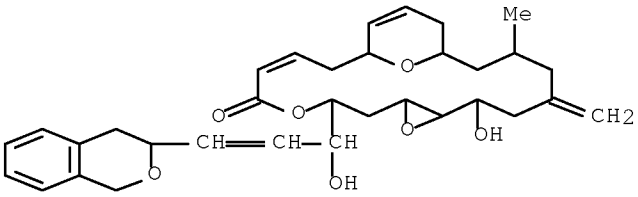


RN 1058707-62-2 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-3-(tetrahydro-4-methyl-2H-pyran-2-yl)-2-propen-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

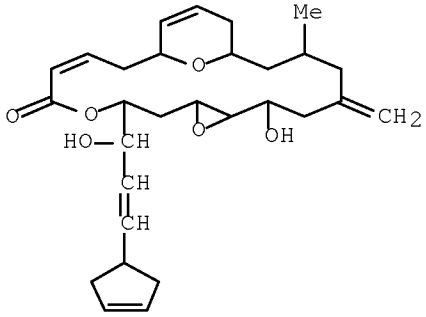


RN 1058707-64-4 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one,

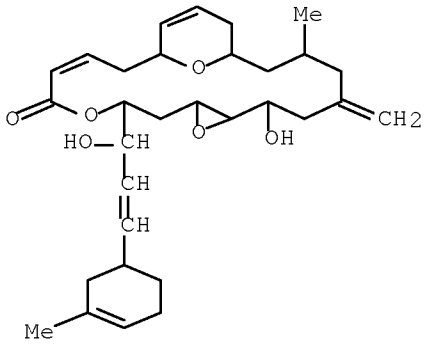
12-[(1S,2E)-3-(3,4-dihydro-1H-2-Benzopyran-3-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 1058707-66-6 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(3-cyclopenten-1-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

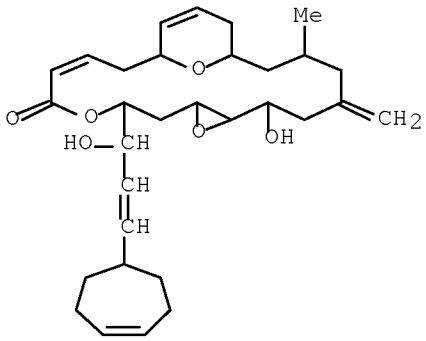


RN 1058707-68-8 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-3-(3-methyl-3-cyclohexen-1-yl)-2-propen-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

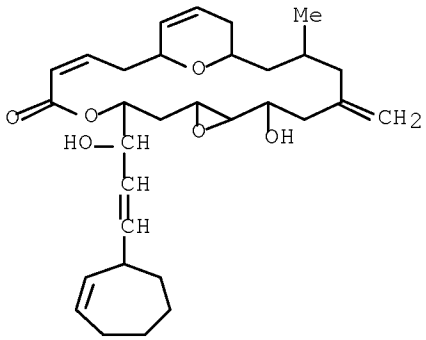


RN 1058707-71-3 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(4-cyclohepten-1-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-

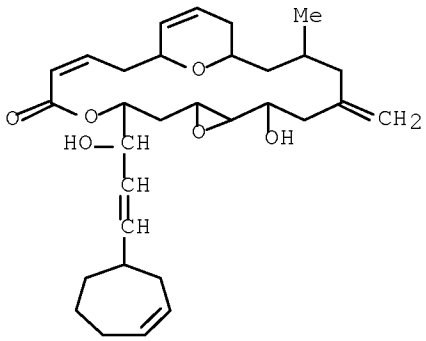
methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 1058707-75-7 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(2-cyclohepten-1-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

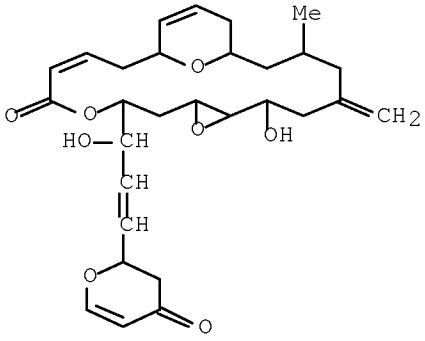


RN 1058707-76-8 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(3-cyclohepten-1-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

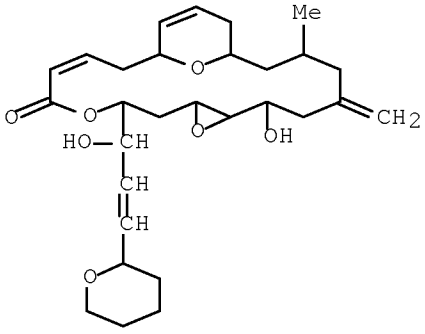


RN 1058707-77-9 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(3,4-dihydro-4-oxo-2H-pyran-2-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 1058707-78-0 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-3-(tetrahydro-2H-pyran-2-yl)-2-propen-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:902328 CAPLUS Full-text
DOCUMENT NUMBER: 149:323034
TITLE: Function-Oriented Synthesis: Biological Evaluation of Laulimalide Analogues Derived from a Last Step Cross Metathesis Diversification Strategy
AUTHOR(S): Mooberry, Susan L.; Hilinski, Michael K.; Clark, Erin A.; Wender, Paul A.
CORPORATE SOURCE: Department of Physiology and Medicine, Southwest Foundation for Biomedical Research, San Antonio, TX, 78245, USA
SOURCE: Molecular Pharmaceutics (2008), 5(5), 829-838
CODEN: MPOHBP; ISSN: 1543-8384
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English

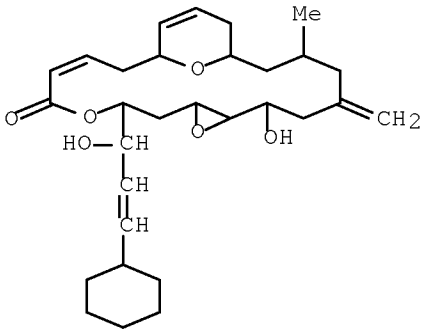
AB Laulimalide is a potent microtubule stabilizing agent and a promising anticancer therapeutic lead. The identification of stable, efficacious and accessible analogs is critical to clin. exploiting this novel lead. To determine which structural features of laulimalide are required for beneficial function and thus for accessing superior clin. candidates, a series of side chain analogs were prepared through a last step cross metathesis diversification strategy and their biol. activities were evaluated. Five analogs, differing in potency from 233 nM to 7.9 μM, effectively inhibit cancer cell proliferation. Like laulimalide, they retain activity against multidrug resistant cells, stabilize microtubules and cause the formation of aberrant mitotic spindles, mitotic accumulation, Bcl-2 phosphorylation and initiation of apoptosis. Structural modifications in the C23-C27 dihydropyran side chain can be made without changing the overall mechanism of action, but it is clear that this subunit has more than a bystander role.

IT 911834-92-9P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(biol. evaluation of laulimalide analogs derived from a last step cross metathesis diversification strategy)

RN 911834-92-9 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-cyclohexyl-1-hydroxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



IT 1049737-05-4

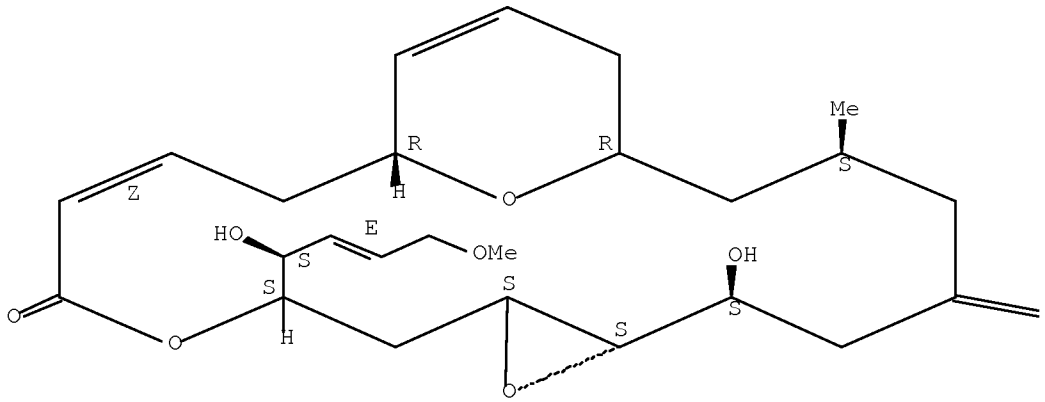
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(biol. evaluation of laulimalide analogs derived from a last step cross metathesis diversification strategy)

RN 1049737-05-4 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-4-methoxy-2-buten-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

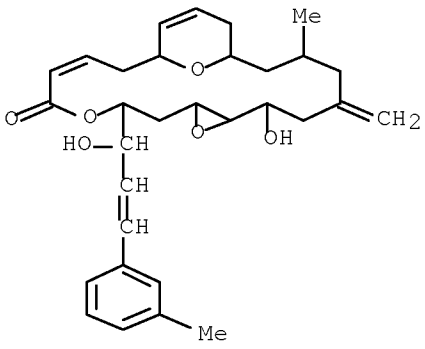
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

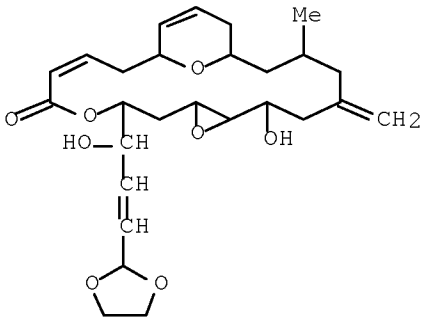


PAGE 1-B

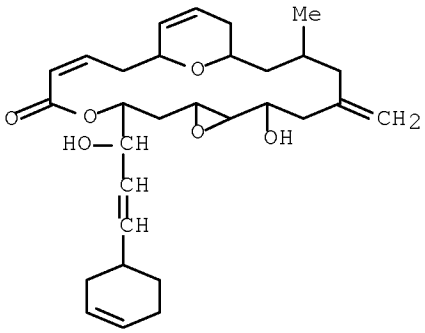
IT 1049737-12-3P 1049737-14-5P 1049737-16-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(biol. evaluation of laulimalide analogs derived from a last step cross metathesis diversification strategy)
RN 1049737-12-3 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-16-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-3-(3-methylphenyl)-2-propen-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 1049737-14-5 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(1,3-dioxolan-2-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



RN 1049737-16-7 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-(3-cyclohexen-1-yl)-1-hydroxy-2-propen-1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

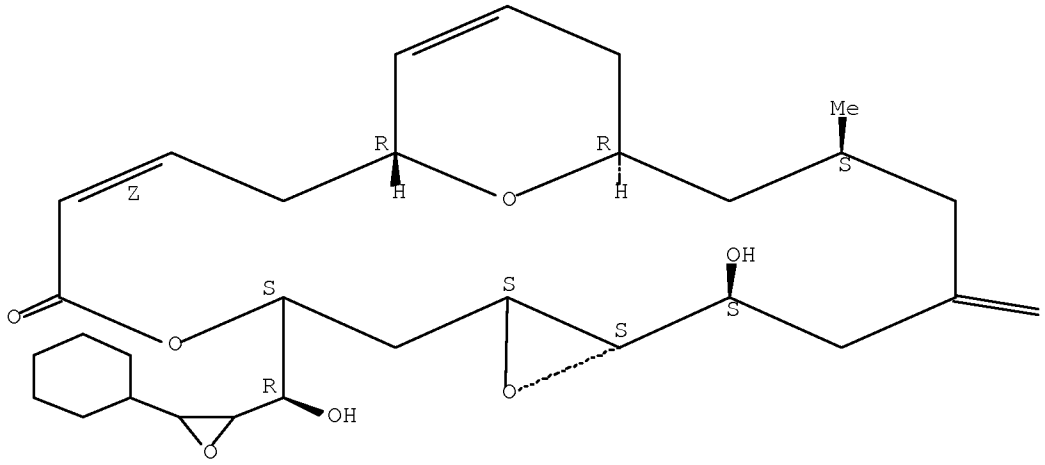


IT 1049737-10-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biol. evaluation of laulimalide analogs derived from a last step cross

metathesis diversification strategy)
RN 1049737-10-1 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(R)-(3-cyclohexyl-2-oxiranyl)hydroxymethyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

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REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:749859 CAPLUS Full-text
DOCUMENT NUMBER: 147:296450
TITLE: Sponge-Derived Fijianolide Polyketide Class: Further Evaluation of Their Structural and Cytotoxicity Properties
AUTHOR(S): Johnson, Tyler A.; Tenney, Karen; Cichewicz, Robert H.; Morinaka, Brandon I.; White, Kimberly N.; Amagata, Taro; Subramanian, Balanehru; Media, Joseph; Mooberry,

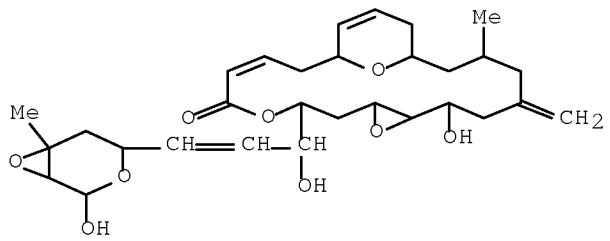
Susan L.; Valeriote, Frederick A.; Crews, Phillip
CORPORATE SOURCE: Department of Chemistry and Biochemistry and Institute for Marine Sciences, University of California, Santa Cruz, CA, 95064, USA
SOURCE: Journal of Medicinal Chemistry (2007), 50(16), 3795-3803
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The sponge-derived polyketide macrolides fijianolides A (I) and B (II), isolaulimalide and laulimalide, have taxol-like microtubule-stabilizing activity, and the latter exhibits potent cytotoxicity. Insight on the biogeog. and phenotypic variations of Cacospongia mycofijiensis is presented that will enable a future study of the biosynthetic pathway that produces the fijianolides. In addition to fijianolides A and B, six new fijianolides, D-I (VII-XII), were isolated, each with modifications to the C-20 side chain of the macrolide ring. Compds. VII-XII exhibited a range of in vitro activities against HCT-116 and MDA-MB-435 cell lines. Fijianolides VIII and X were shown to disrupt interphase and mitotic division, but were less potent than II. An in vivo evaluation of II using tumor-bearing severe combined immuno-deficiency mice demonstrated significant inhibition of growth in HCT-116 tumors over 28 days.

IT 947340-18-3P, Fijianolide G
RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(structure and cytotoxicity of sponge-derived fijianolide polyketide class)

RN 947340-18-3 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-3-[(1R,2S,4S,6R)-2-hydroxy-6-methyl-3,7-dioxabicyclo[4.1.0]hept-4-yl]-2-propen-1-yl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)

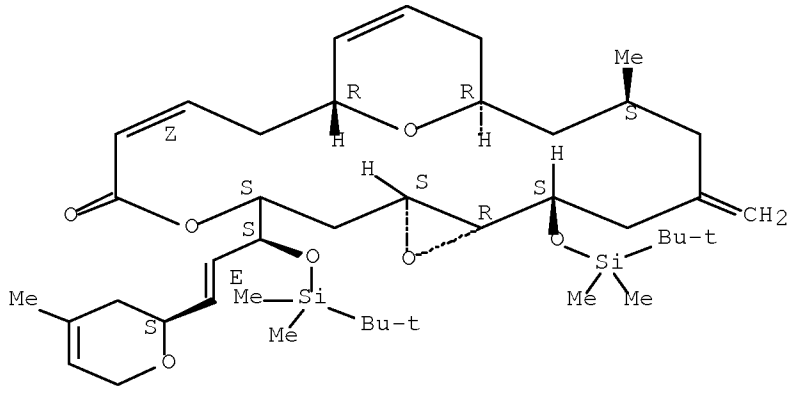


REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 5 OF 24 CAPLUS

ACCESSION NUMBER: 2007:111510 CAPLUS Full-text
DOCUMENT NUMBER: 149:331755
TITLE: Product class 6: lactones
AUTHOR(S): Maier, M. E.
CORPORATE SOURCE: Institut fuer Organische Chemie, Universitaet Tuebingen, Tuebingen, 72076, Germany
SOURCE: Science of Synthesis (2006), 20b, 1421-1551
CODEN: SSCYJ9
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review of methods to prepare lactones and their applications to organic synthesis.
IT 439867-75-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(review preparation of lactones and their applications to organic synthesis)
RN 439867-75-1 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-7-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 602 THERE ARE 602 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:1167409 CAPLUS Full-text
DOCUMENT NUMBER: 146:155286
TITLE: 3-D QSAR studies of microtubule stabilizing antimitotic agents towards six cancer cell lines
AUTHOR(S): Mohanraj, Sumithra; Doble, Mukesh
CORPORATE SOURCE: Department of Biotechnology, Indian Institute of Technology, Madras, Chennai, 600036, India
SOURCE: QSAR & Combinatorial Science (2006), 25(10), 952-960
CODEN: QCSSAU; ISSN: 1611-020X
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal

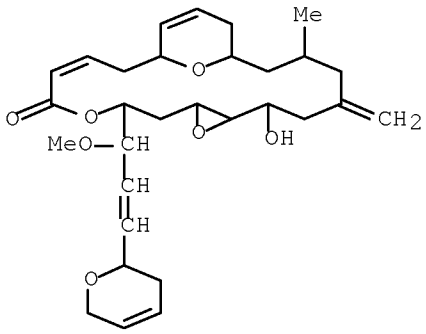
LANGUAGE: English

AB The antimitotic agent paclitaxel continues to play an important role in cancer chemotherapy. However, its inefficacy on certain resistant cells and toxic side effects had led to the search for new drugs with improved biol. activity. Here the QSAR models for microtubule stabilizing anticancer agents were performed to correlate their physicochem. properties with biol. activity. Single and multiple linear regression models for six cancer cell lines were obtained with R2 ≥ 0.65 and q2pre ≥ 0.6. Mol. mechanics energy and log P of the mols. account for the activity of taxanes towards B16 melanoma and breast cancer cells, resp. The lowest unoccupied MOs and the number of nitrogen atoms in the structure account for the biol. activity of epothilone derivs. and rest of the drugs towards ovarian cells. The relation between the structural properties of microtubule stabilizing antimitotic compds. and their activities on different cell lines are investigated in this paper.

IT 920493-66-9, Laulimalide 2
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(QSAR studies of microtubule stabilizing antimitotic agents)

RN 920493-66-9 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-2H-pyran-2-yl]-1-methoxy-2-propen-1-yl]-7-hydroxy-3-methYl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:1110729 CAPLUS Full-text

DOCUMENT NUMBER: 146:62511

TITLE: Synthetic studies on a phenyl-laulimalide analogue

AUTHOR(S): Faveau, Christelle; Mondon, Martine; Gesson, Jean-Pierre; Mahnke, Tobias; Gebhardt, Sandra; Koert, Ulrich

CORPORATE SOURCE: CNRS UMR 6514, Universite de Poitiers, Poitiers, 86022, Fr.

SOURCE: Tetrahedron Letters (2006), 47(47), 8305-8308
CODEN: TELEAY; ISSN: 0040-4039

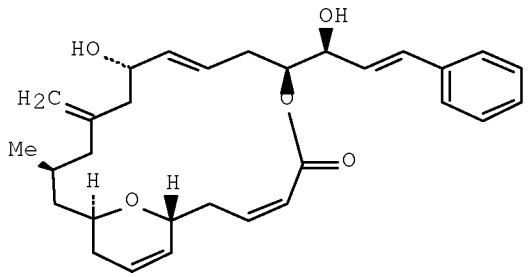
PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 146:62511

GI



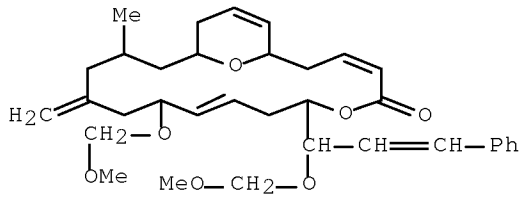
I

AB Analog I of the paclitaxel-like antimicrotubule agent laulimalide with a Ph in place of the dihydropyran has been synthesized. Keys steps include the coupling of fragments C1-C14 and C15-C28 via a stereoselective intermol. allylboration and macrolactonization via Yamaguchi's protocol.

IT 916771-88-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthetic studies on a phenyl-laulimalide analog)

RN 916771-88-5 CAPLUS

CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 11-(methoxymethoxy)-7-[(1S,2E)-1-(methoxymethoxy)-3-phenyl-2-propen-1-yl]-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

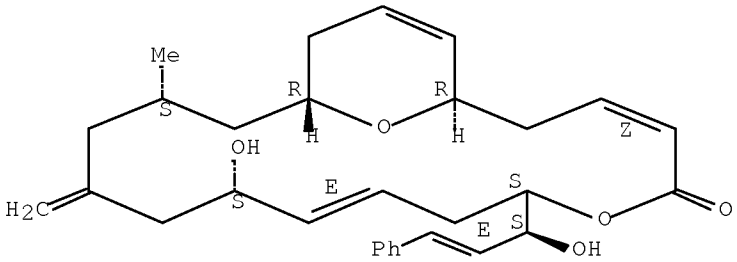


IT 916771-69-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthetic studies on a phenyl-laulimalide analog)

RN 916771-69-2 CAPLUS

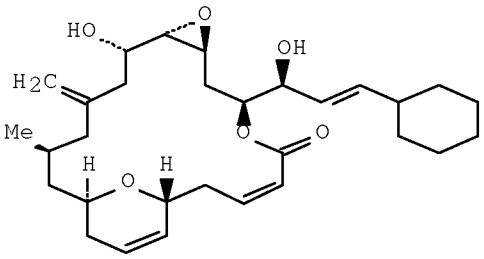
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 11-hydroxy-7-[(1S,2E)-1-hydroxy-3-phenyl-2-propen-1-yl]-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:797947 CAPLUS Full-text
DOCUMENT NUMBER: 145:418821
TITLE: Pharmacophore Mapping in the Laulimalide Series: Total Synthesis of a Vinylogue for a Late-Stage Metathesis Diversification Strategy
AUTHOR(S): Wender, Paul A.; Hilinski, Michael K.; Skaanderup, Philip R.; Soldermann, Nicolas G.; Mooberry, Susan L.
CORPORATE SOURCE: Departments of Chemistry and Molecular Pharmacology, Stanford University, Stanford, CA, 94305-5080, USA
SOURCE: Organic Letters (2006), 8(18), 4105-4108
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:418821
GI

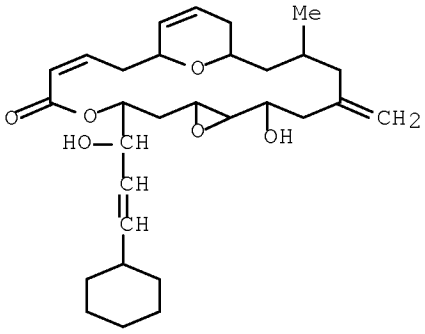


I

AB An efficient synthesis of the macrocyclic core I of laulimalide with a pendant vinyl group at C20 is described, allowing for late-stage introduction of various side chains through a selective and efficient cross metathesis diversification step. Representative analogs reported herein are the first to contain modifications to only the side chain dihydropyran of laulimalide and des-epoxy laulimalide. This step-economical strategy enables the rapid synthesis of new analogs using alkenes as an inexpensive, abundantly available diversification feedstock.

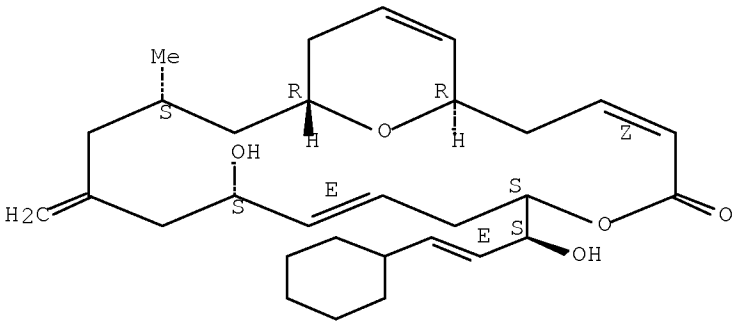
IT 911834-92-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(total synthesis of a laulimalide vinylogue for a late-stage metathesis

diversification strategy as potential human anticancer agent)
RN 911834-92-9 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-cyclohexyl-1-hydroxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



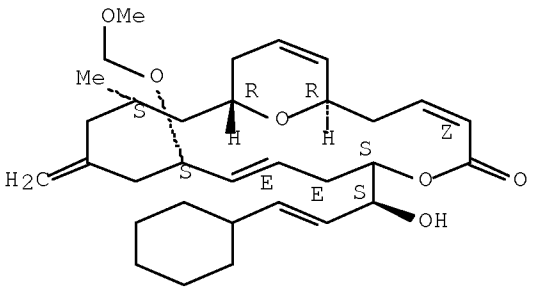
IT 911834-91-8P 911834-96-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of a laulimalide vinylogue for a late-stage metathesis diversification strategy as potential human anticancer agent)
RN 911834-91-8 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-cyclohexyl-1-hydroxy-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 911834-96-3 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-cyclohexyl-1-hydroxy-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:737763 CAPLUS Full-text
DOCUMENT NUMBER: 139:261091
TITLE: Preparation of laulimalide and epothilone derivatives as microtubule stabilizing compounds
INVENTOR(S): Ghosh, Arun K.
PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois, USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076445	A2	20030918	WO 2003-US6457	20030304
WO 2003076445	A3	20040108		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2478087	A1	20030918	CA 2003-2478087	20030304
AU 2003216491	A1	20030922	AU 2003-216491	20030304
EP 1483267	A2	20041208	EP 2003-744154	20030304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005521694	T	20050721	JP 2003-574661	20030304
US 20030203929	A1	20031030	US 2003-382261	20030305
US 7109235	B2	20060919		
MX 2004008630	A	20041206	MX 2004-8630	20040906

PRIORITY APPLN. INFO.:	US 2002-362499P	P	20020307
	WO 2003-US6457	W	20030304

OTHER SOURCE(S): MARPAT 139:261091
GI

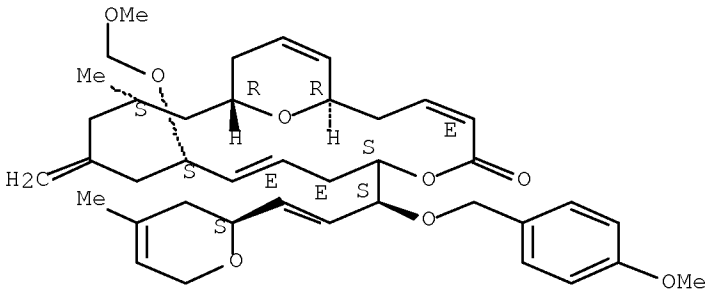
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Laulimalide and epothilone derivs., e.g., I [R1 = H, ORa, C1-3-alkyl; R2 = C3-7-heterocyclolalkyl, C3-7-heterocyclolalkenyl, C3-7-cyclolalkyl, C3-7-cyclolalkenyl,C3-7-alkylene-ORa, ORa, C3-7-cyclolalkylene-N(Ra)2, N(Ra)2, aryl, heteroaryl; R3 = heteroaryl, aryl, C3-7-heterocyclolalkyl, C3-7-heterocyclolalkenyl; R4 = C1-4-alkyl, ORa, C3-7-cycloalkyl, C3-7-heterocyclolalkyl, aryl, heteroaryl; X, Y = CH2, O, NRa, S; Ra = H, C1-4-alkyl, C2-4-alkenyl, C2-4-alkynyl, heteroaryl, aryl; Z = (CH2)n; n = 0, 1], II, III, IV, V, VI and a pharmaceutically acceptable salt, solvate or prodrug thereof, useful as microtubule stabilizing agents, and in the treatment of cancers are disclosed. Methods of making the compds. and using the compds. as therapeutic agents in treating cancers also are disclosed. Thus, trans-desoxylaulimalide I [R1 = β-OH, R2 = R', R4 = Me, X = Y = O, Z = CH2] was prepared from (E)-R'CH:CHCH2CH[OH-(S)](CH2)2SO2Ph and {6-[(R)-Me3CSiMe2O(CH2)2]-3,6-dihydropyran-2R-yl}CH2CH[Me-(S)]CH2C(:CH2)CH2CH[OCH2OMe-(S)]CHOin 12 steps. Trans-desoxylaulimalide was tested for cytotoxicity [IC50 = 360 nM vs. human MCF-7 breast cancer cells].

IT 312695-86-6 312695-87-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(O-deprotection of; preparation of laulimalide and epothilone derivs. as microtubule stabilizing compds. with antitumor activity)

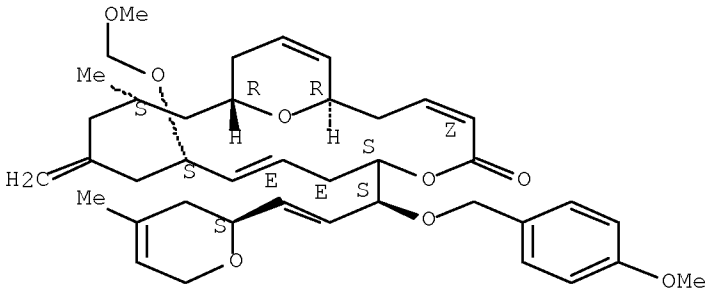
RN 312695-86-6 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(4-methoxyphenyl)methoxy]-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3E,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 312695-87-7 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(4-methoxyphenyl)methoxy]-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



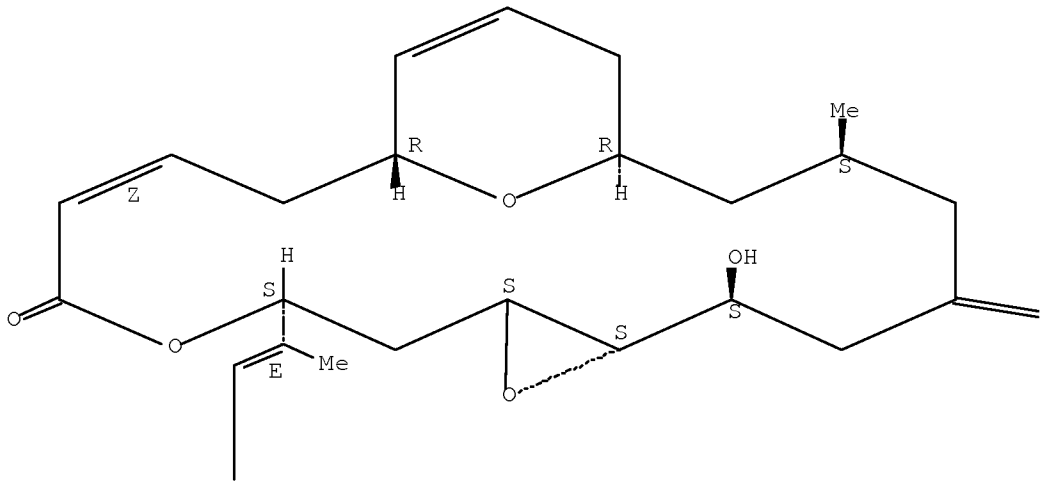
IT 600145-61-7P 600145-62-8P 600145-64-0P
600145-65-1P 600145-66-2P 600145-75-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of laulimalide and epothilone derivs. as microtubule stabilizing compds. with antitumor activity)

RN 600145-61-7 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-3-methyl-5-methylene-12-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

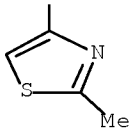
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



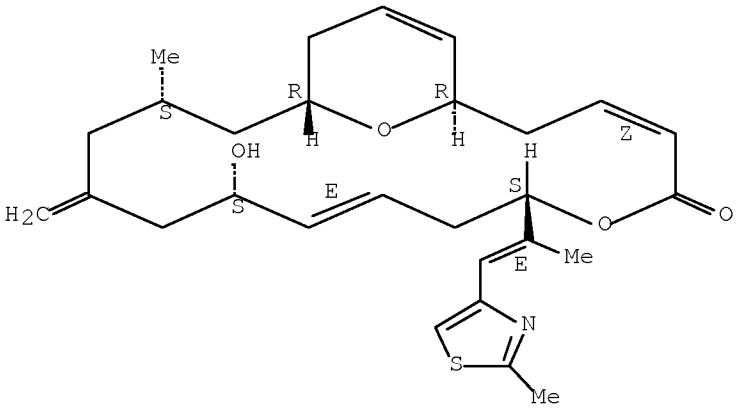
PAGE 1-B

PAGE 2-A



RN 600145-62-8 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 11-hydroxy-15-methyl-13-methylene-7-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

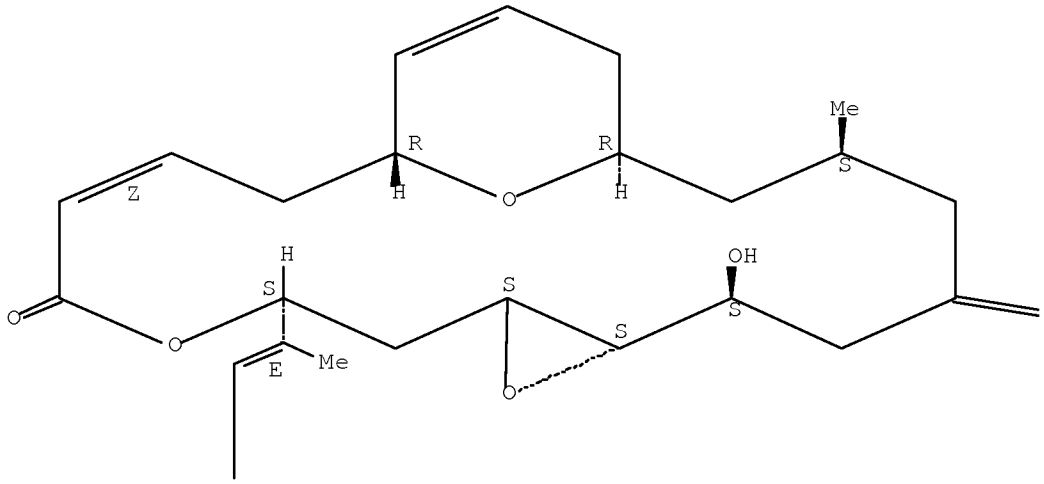
Absolute stereochemistry.
Double bond geometry as shown.



RN 600145-64-0 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-3-methyl-5-methylene-12-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

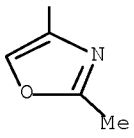
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

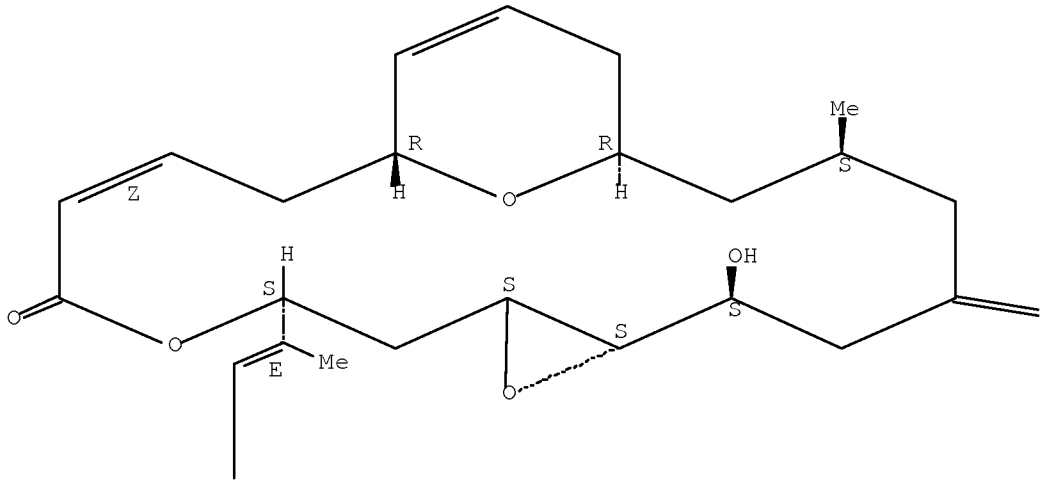
PAGE 2-A



RN 600145-65-1 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-3-methyl-5-methylene-12-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

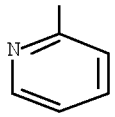
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

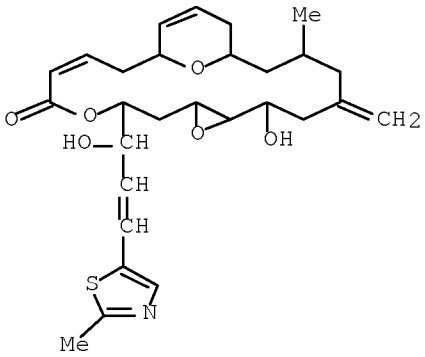


PAGE 1-B

PAGE 2-A

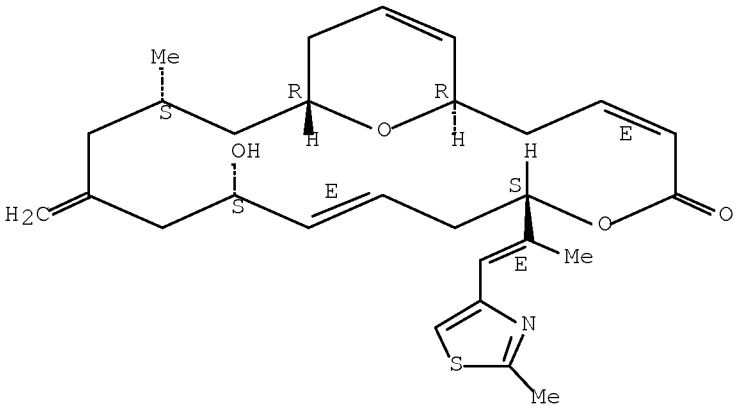


RN 600145-66-2 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 7-hydroxy-12-[(1S,2E)-1-hydroxy-3-(2-methyl-5-thiazolyl)-2-propenyl]-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



RN 600145-75-3 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 11-hydroxy-15-methyl-13-methylene-7-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3E,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

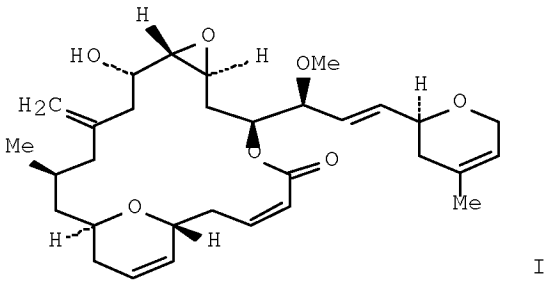
Absolute stereochemistry.
Double bond geometry as described by E or Z.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:669822 CAPLUS Full-text
DOCUMENT NUMBER: 139:337809
TITLE: Synthesis and Biological Evaluation of (-)-Laulimalide Analogues
AUTHOR(S): Wender, Paul A.; Hegde, Sayee G.; Hubbard, Robert D.; Zhang, Lei; Mooberry, Susan L.
CORPORATE SOURCE: Department of Chemistry, Stanford University, Stanford, CA, 94305, USA
SOURCE: Organic Letters (2003), 5(19), 3507-3509
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:337809

GI



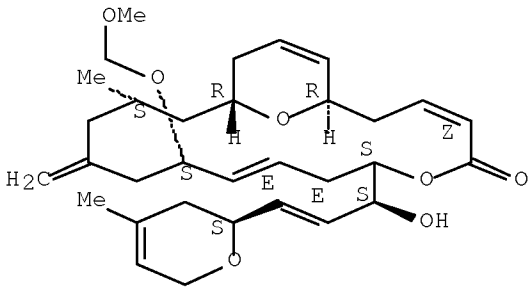
I

AB The syntheses of five laulimalide analogs, e.g. I, are described, incorporating modifications at the C16-C17-epoxide, the C20-alc., as well as the C1-C3-enoate of the parent natural product. The resultant analogs are active in drug-sensitive HeLa and MDA-MB-435 cell lines. Significantly, like laulimalide, these analogs are poor substrates for the drug transport protein P-glycoprotein (Pgp) and are thus effective against Taxol-resistant cell lines.

IT 438222-74-3P 616201-10-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. evaluation of (-)-laulimalide analogs)

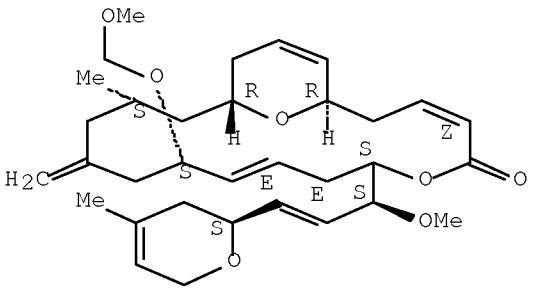
RN 438222-74-3 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 616201-10-6 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

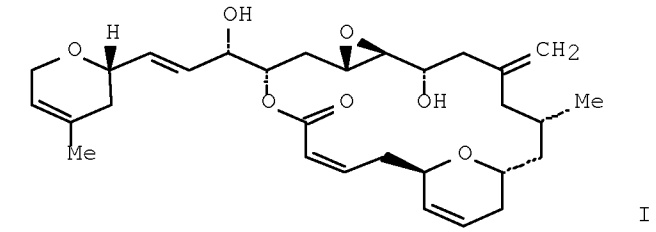


REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

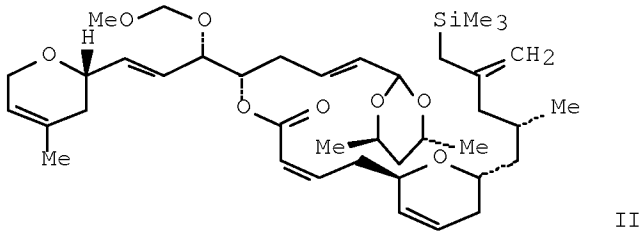
L40 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:238326 CAPLUS Full-text
DOCUMENT NUMBER: 138:271451
TITLE: Preparation of laulimalide and its derivatives for pharmaceutical uses
INVENTOR(S): Mulzer, Johann; Enev, Valentin S.
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 58 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1295886	A1	20030326	EP 2001-250331	20010920
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2003024975	A1	20030327	WO 2002-EP10546	20020919
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002335314	A1	20030401	AU 2002-335314	20020919
PRIORITY APPLN. INFO.:			EP 2001-250331 A	20010920
			WO 2002-EP10546 W	20020919

OTHER SOURCE(S): MARPAT 138:271451
GI



I



II

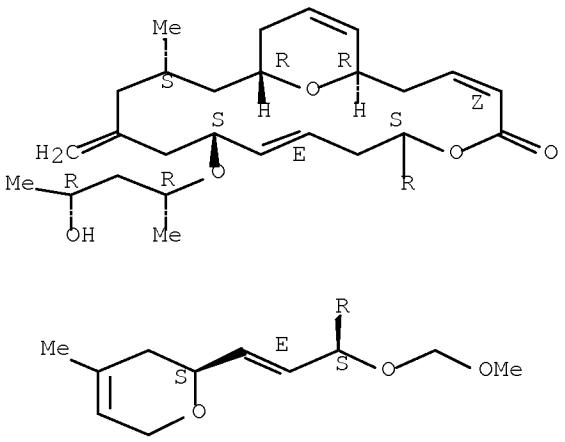
AB Laulimalide (I) and its derivs. were prepared for a variety of therapeutic uses, such as treatment of cancer, such as solid tumors and leukemia, autoimmune diseases, such as psoriasis, and multiple sclerosis, chemotherapeutically induced alopecia and mucositis, cardiovascular diseases, such as stenosis, arteriosclerosis and restenosis, infectious diseases caused by unicellular parasites, such as Trypanosoma, Toxoplasma or Plasmodium, or nephrol. diseases caused by fungi, such as glomerulonephritis, chronical neurodegenerative diseases, such as Huntington's disease, amyotropical lateral sclerosis, Parkinson disease, AIDS dementia and Alzheimer's diseases, acute neurodegenerative disease, such as ischemia of the brain and neurotrauma, viral infections, such as Cytomegalovirus infections, herpes, hepatitis B and C, and HIV diseases. Thus, laulimalide was prepared via a multistep synthetic sequence which included formation of the core macrocyclic ring by intramol. cyclization of protected aldehyde II using EtAlCl2 in CH2Cl2. Biol. testing data fop the prepared laulimalide derivs. were not presented.

IT 503064-81-1P 503064-82-2P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of laulimalide and its derivs. for variety of pharmaceutical uses)

RN 503064-81-1 CAPLUS

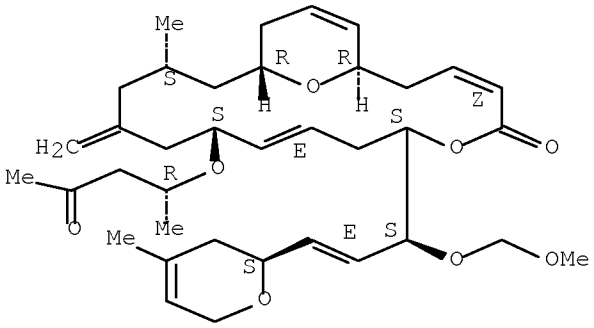
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propen-1-yl]-11-[(1R,3R)-3-hydroxy-1-methylbutoxy]-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 503064-82-2 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propen-1-yl]-15-methyl-13-methylene-11-[(1R)-1-methyl-3-oxobutoxy]-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

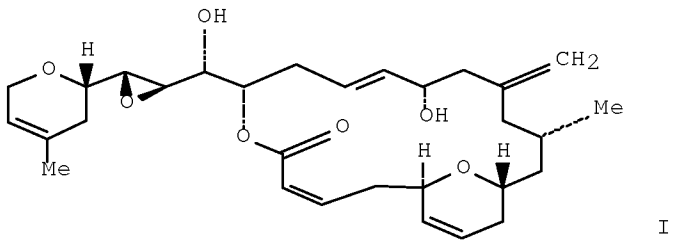
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:235688 CAPLUS Full-text
DOCUMENT NUMBER: 138:385202
TITLE: Total Synthesis of the Microtubule Stabilizing Antitumor Agent Laulimalide and Some Nonnatural Analogues: The Power of Sharpless' Asymmetric Epoxidation
AUTHOR(S): Ahmed, Anjum; Hoegenauer, E. Kate; Enev, Valentin S.; Hanbauer, Martin; Kaehlig, Hanspeter; Oehler, Elisabeth; Mulzer, Johann
CORPORATE SOURCE: Institut fuer Organische Chemie, Universitaet Wien, Vienna, A-1090, Austria
SOURCE: Journal of Organic Chemistry (2003), 68(8), 3026-3042
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:385202
GI



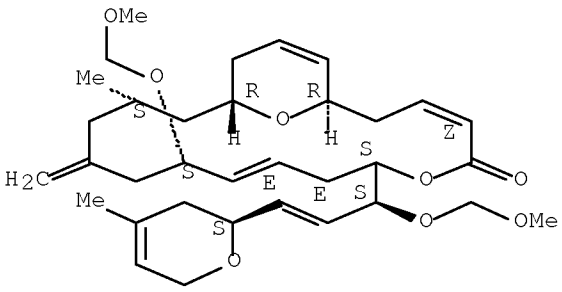
I

AB Three different routes are described for the synthesis of deoxylaulimalide, which is the immediate precursor of the marine sponge metabolite laulimalide. These routes mainly differ with respect to their ring closing step. Thus, route 1 uses a Still-Gennari olefination, route 2 a Yamaguchi lactonization, and route 3 an intramol. allylsilane-aldehyde addition for establishing the macrocyclic structure. The unprotected deoxy derivative was subjected to Sharpless' asym. epoxidn. (SAE). With (R,R)-tartrate the 16,17-epoxide laulimalide is formed selectively, whereas (S,S)-tartrate generates the 21,22-epoxide I. This demonstrates the high reagent control involved in the SAE process, which in this case is used to achieve high stereo- and regioselectivity. Laulimalide and some derivs. thereof were tested with respect to antitumor activity and compared to standard compds. paclitaxel and epothilone B.

IT 385809-26-7P 385809-28-9P 503064-81-1P
503064-82-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn of laulimalide and deoxylaulimalide from small chiral compds. via key Still-Gennari olefination, Yamaguchi lactonization, intramol. addition cyclization strategies or Sharpless epoxidn. and evaluation of their antitumor activity)

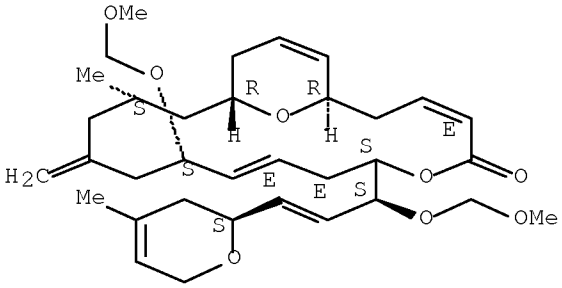
RN 385809-26-7 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



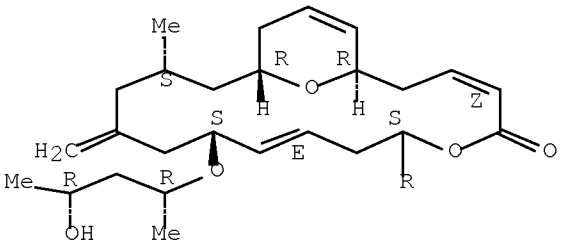
RN 385809-28-9 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3E,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

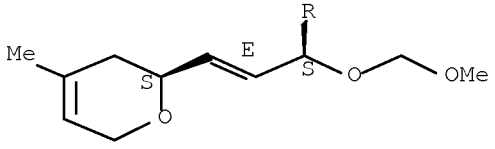
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 503064-81-1 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propen-1-yl]-11-[(1R,3R)-3-hydroxy-1-methylbutoxy]-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

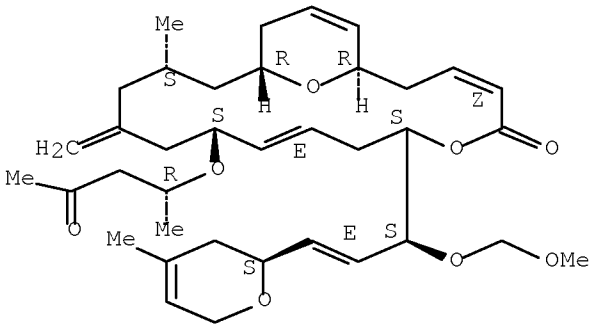
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.





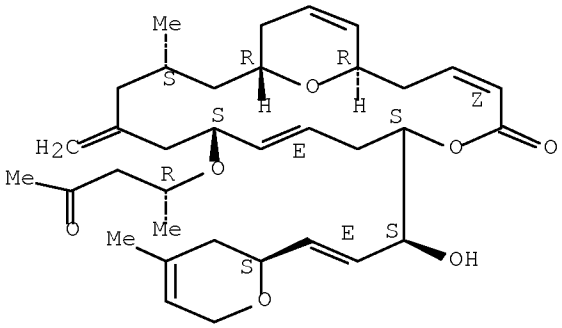
RN 503064-82-2 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one,
7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-
2-propen-1-yl]-15-methyl-13-methylene-11-[(1R)-1-methyl-3-oxobutoxy]-,
(1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



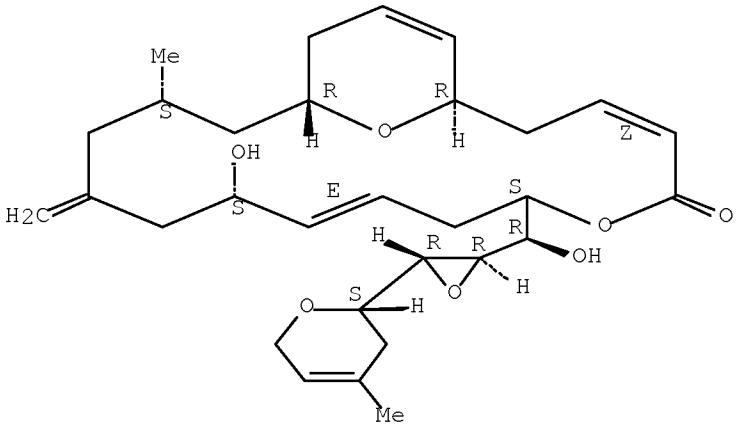
IT 527742-89-8P 527742-91-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn of laulimalide and deoxylaulimalide from small chiral compds.
via key Still-Gennari olefination, Yamaguchi lactonization, intramol.
addition cyclization strategies or Sharpless epoxidn. and evaluation of
their antitumor activity)
RN 527742-89-8 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one,
7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-
propenyl]-15-methyl-13-methylene-11-[(1R)-1-methyl-3-oxobutoxy]-,
(1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 527742-91-2 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one,
7-[(R)-[(2R,3R)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-
yl]oxiranyl]hydroxymethyl]-11-hydroxy-15-methyl-13-methylene-,
(1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 170 THERE ARE 170 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:816741 CAPLUS Full-text
DOCUMENT NUMBER: 138:39137
TITLE: A de Novo Enantioselective Total Synthesis of (-)-Laulimalide
AUTHOR(S): Nelson, Scott G.; Cheung, Wing S.; Kassick, Andrew J.; Hilfiker, Mark A.
CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SOURCE: Journal of the American Chemical Society (2002), 124(46), 13654-13655
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:39137

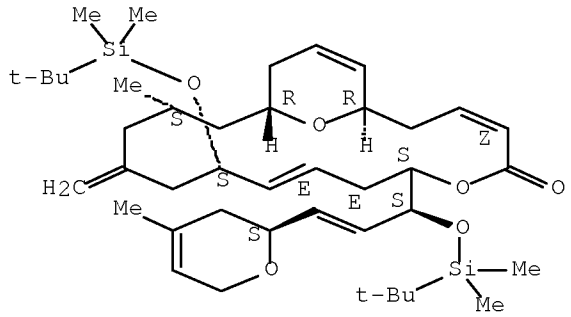
AB An enantioselective total synthesis of the naturally occurring anticancer agent (-)-laulimalide is described. The synthesis is characterized by extensive use of new reaction methodologies based on catalytic asym. acyl halide-aldehyde cyclocondensation (AAC) reactions and transformations of the derived enantioenriched β-lactones. The synthesis also incorporates a unique allenylstannane glycal acetate alkylation and chemoselective ring-closing metathesis reaction.

IT 449142-46-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of (-)-laulimalide from acetone via catalytic asym. acyl halide-aldehyde cyclocondensation, allenylstannane glycal acetate alkylation and chemoselective ring-closing metathesis reactions)

RN 449142-46-5 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-15-methyl-13-methylene-,

(1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



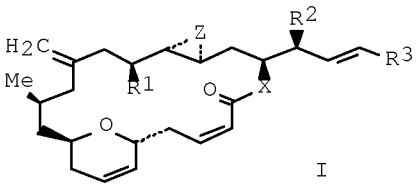
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:637675 CAPLUS Full-text
DOCUMENT NUMBER: 137:185361
TITLE: Preparation of laulimalide derivatives for treating diseases of cellular hyperproliferation
INVENTOR(S): Ashley, Gary; Metcalf, Brian
PATENT ASSIGNEE(S): Kosan Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

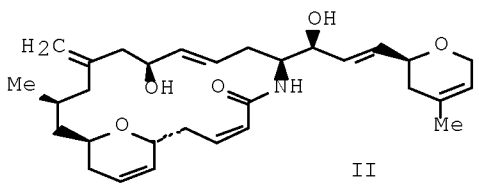
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064589	A1	20020822	WO 2002-US3706	20020208
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2436195	A1	20020822	CA 2002-2436195	20020208
AU 2002236982	A1	20020828	AU 2002-236982	20020208
US 20020128471	A1	20020912	US 2002-71839	20020208
US 6670389	B2	20031230		
EP 1358186	A1	20031105	EP 2002-703356	20020208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004518728	T	20040624	JP 2002-564520	20020208
US 20030195181	A1	20031016	US 2003-364111	20030210
US 6815463	B2	20041109		

PRIORITY APPLN. INFO.:	US 2001-267603P	P	20010209
	US 2002-71839	A1	20020208
	WO 2002-US3706	W	20020208

OTHER SOURCE(S): MARPAT 137:185361
GI



I



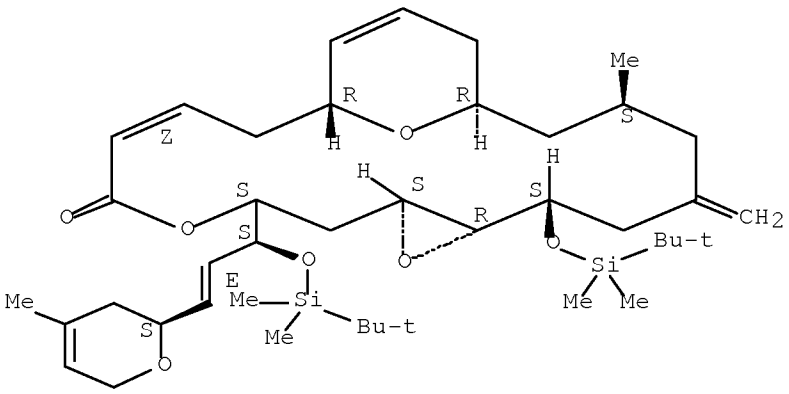
II

AB Laulimalide derivs., such as I [X = O, NH; Z = O, CH2, a bond; R1, R2 = H, OH, alkoxy; R3 = (un)substituted cyclohexyl, cyclohexenyl, Ph, pyridyl, thiazolyl, pyranyl], were prepared for their use in the treatment of diseases characterized by cellular hyperproliferation. Thus, 16,17-desoxylaulimalide lactam (II) was prepared via a multistep synthetic sequence starting from N-methoxy-N-methyl-2-hydroxy-4-(phenylsulfonyl)- butyramide, phenylacetylene, and (2S,6S,8R,12R)-8,12-epoxy-2- (methoxymethoxy)-6-methyl-4-methylidene-14-(tert- butyldimethylsilyloxy)tetradec-10-enal.

IT 439867-75-1P 449142-46-5P 449142-53-4P
449142-54-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of laulimalide derivs. for their use in the treatment of diseases characterized by cellular hyperproliferation)

RN 439867-75-1 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-7-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (CA INDEX NAME)

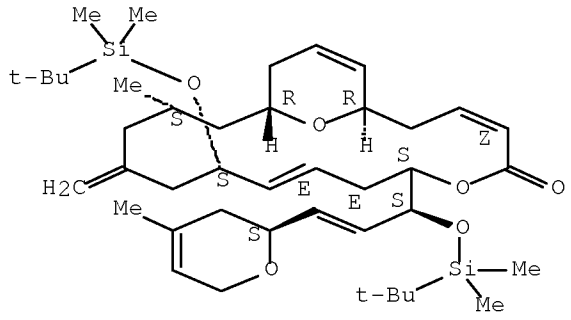
Absolute stereochemistry.
Double bond geometry as shown.



RN 449142-46-5 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-15-methyl-13-methylene-,

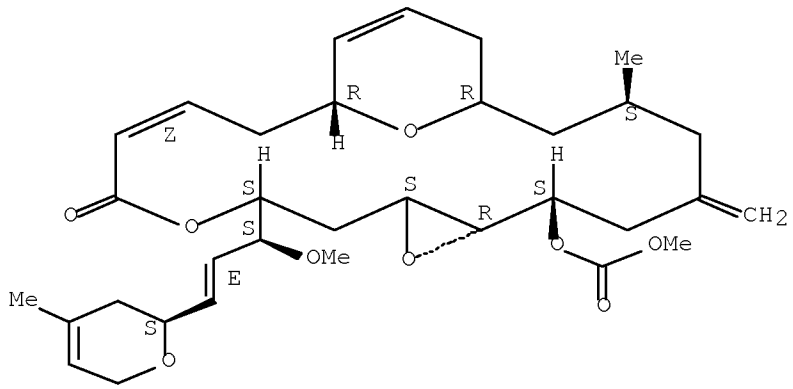
(1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



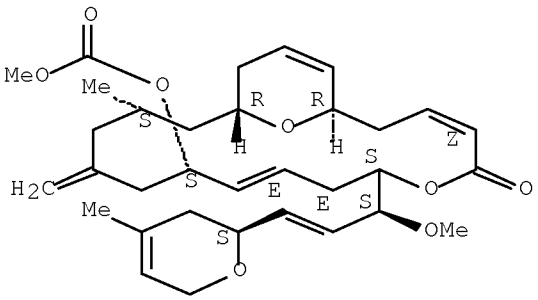
RN 449142-53-4 CAPLUS
CN Carbonic acid, (1R,3S,7S,8R,10S,12S,15Z,18R)-12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-3-methyl-5-methylene-14-oxo-9,13,22-trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-7-yl methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 449142-54-5 CAPLUS
CN Carbonic acid, (1R,3Z,7S,9E,11S,15S,17R)-7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-15-methyl-13-methylene-5-oxo-6,21-dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-11-yl methyl ester (9CI) (CA INDEX NAME)

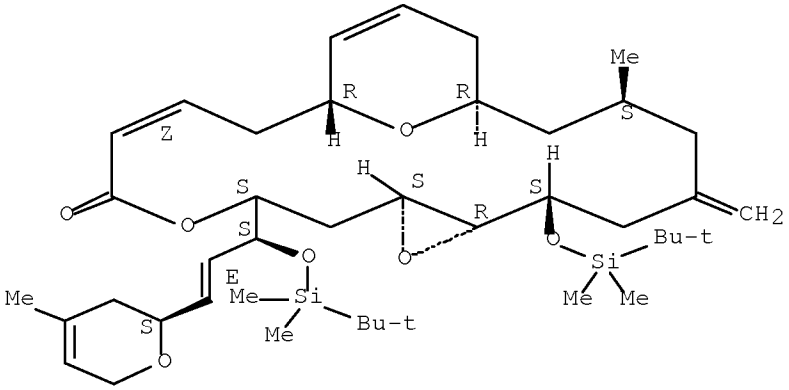
Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:456619 CAPLUS Full-text
DOCUMENT NUMBER: 137:279014
TITLE: Synthesis of (-)-laulimalide: an agent for microtubule stabilization
AUTHOR(S): Williams, David R.; Mi, Liang; Mullins, Richard J.; Stites, Ryan E.
CORPORATE SOURCE: Department of Chemistry, Indiana University, Bloomington, IN, 47405-7102, USA
SOURCE: Tetrahedron Letters (2002), 43(27), 4841-4844
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:279014
AB An enantioselective synthesis of a protected (-)-laulimalide is described. Key reactions include a convergent allylation coupling reaction, asym. conjugate addition, the allenylstannane Ferrier reaction and a chelation-controlled alkenylzinc addition as the basis for stereocontrol in critical elements of chirality.
IT 439867-75-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of (-)-laulimalide from a N-enoyloxazolidinone via allylation coupling, asym. conjugate addition, the allenylstannane Ferrier reaction and a chelation-controlled alkenylzinc addition reaction)
RN 439867-75-1 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-7-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:332741 CAPLUS Full-text
DOCUMENT NUMBER: 137:63109
TITLE: Asymmetric Total Synthesis of (-)-Laulimalide: Exploiting the Asymmetric Glycolate Alkylation Reaction
AUTHOR(S): Crimmins, Michael T.; Stanton, Matthew G.; Allwein, Shawn P.
CORPORATE SOURCE: Department of Chemistry, Venable and Kenan Laboratories of Chemistry, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599-3290, USA
SOURCE: Journal of the American Chemical Society (2002), 124(21), 5958-5959
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:63109
GI

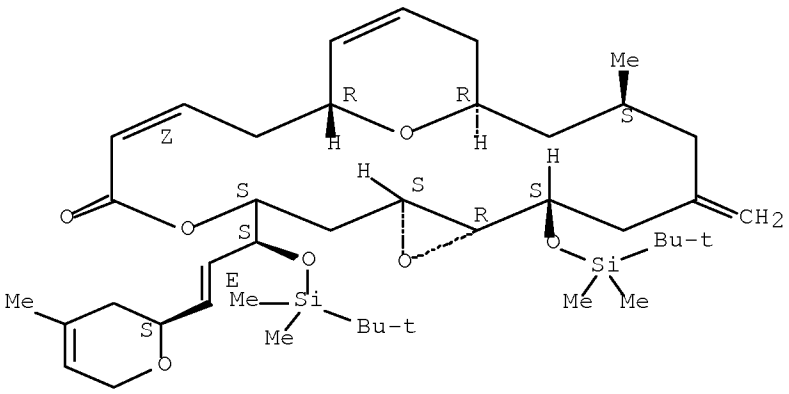
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A concise total synthesis of the potent antitumor macrolide (-)-laulimalide (I) is described. The observation that homoallylic (or latent homoallylic) C-O bonds are present at C5, C9, C15, C19, and C23 led to the strategic decision to rely heavily on the asym. glycolate alkylation to construct both the C1-C14 fragment II and the C15-C27 subunit III. A diastereoselective addition of a C1-C14 allylstannane to a C15-C27 α,β-epoxyaldehyde served to join the two advanced fragments. A Mitsunobu macrolactonization of hydroxy acid IV avoided isomerization of the sensitive 2,3-Z-enoate, which has been observed in base-catalyzed macrolactonizations. Removal of two TBS protecting groups to reveal the C15 and C20 hydroxyls occurred without rearrangement to isolaulimalide.

IT 439867-75-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. total synthesis of (-)-laulimalide via the asym. glycolate

alkylation reaction)
RN 439867-75-1 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-propenyl]-7-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

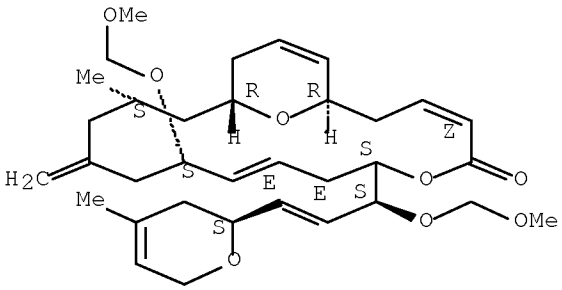


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:303855 CAPLUS Full-text
DOCUMENT NUMBER: 137:154792
TITLE: Total synthesis of the antitumor agent (-)-laulimalide
AUTHOR(S): Mulzer, Johann; Hanbauer, Martin
CORPORATE SOURCE: Institut fur Organische Chemie, Universitat Wien, Vienna, A-1090, Austria
SOURCE: Tetrahedron Letters (2002), 43(18), 3381-3383
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:154792
AB A stereocontrolled synthesis of (-)-laulimalide is described. Key steps are an allylsilane addition to a chiral acetal as the major coupling step and a Yamaguchi macrolactonization for ring closure.
IT 385809-26-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of the antitumor agent (-)-laulimalide via an allylsilane addition to a chiral acetal as the major coupling step and a Yamaguchi macrolactonization for ring closure)
RN 385809-26-7 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

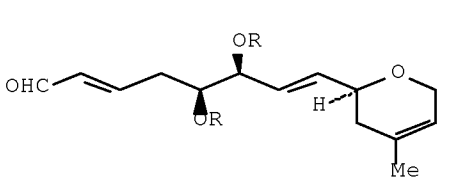
Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.

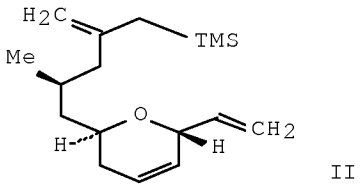


REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:287554 CAPLUS Full-text
DOCUMENT NUMBER: 137:47042
TITLE: Total Synthesis of (-)-Laulimalide
AUTHOR(S): Wender, Paul A.; Hegde, Sayee G.; Hubbard, Robert D.; Zhang, Lei
CORPORATE SOURCE: Department of Chemistry, Stanford University, Stanford, CA, 94305-5080, USA
SOURCE: Journal of the American Chemical Society (2002), 124(18), 4956-4957
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:47042
GI



I



II

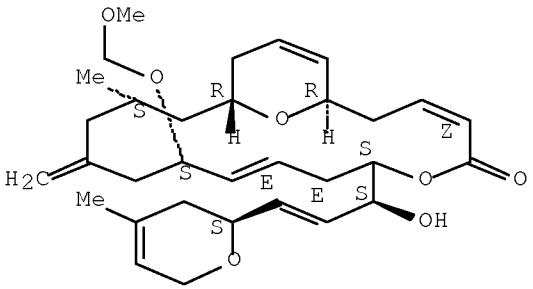
AB A flexible and convergent asym. synthesis of (-)-laulimalide is described. This synthesis featured a highly diastereoselective Sakurai reaction of I (R = SiMe2CMe3) with II and a regioselective macrolactonization of an unprotected vicinal diol. (-)-Laulimalide was synthesized in 25 steps (longest linear; 36 overall) in 3.5% overall yield, providing a uniquely short and efficient route to it and its analogs.

IT 438222-74-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (-)-laulimalide via an asym. Sakurai coupling and a regioselective macrolactonization)

RN 438222-74-3 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-

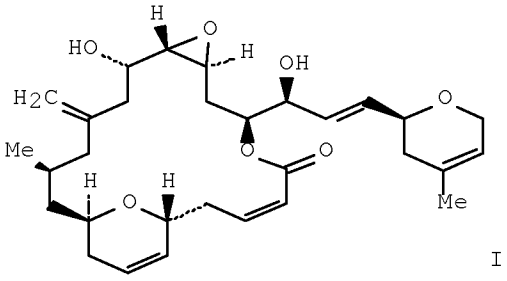
propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-,
(1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

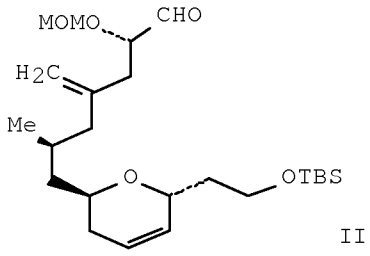


REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

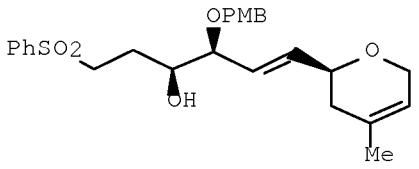
L40 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:869107 CAPLUS Full-text
DOCUMENT NUMBER: 136:151030
TITLE: Total Synthesis of Microtubule-Stabilizing Agent (-)-Laulimalide
AUTHOR(S): Ghosh, Arun K.; Wang, Yong; Kim, Joseph T.
CORPORATE SOURCE: Department of Chemistry, University of Illinois at Chicago, Chicago, IL, 60607, USA
SOURCE: Journal of Organic Chemistry (2001), 66(26), 8973-8982
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:151030
GI



I



II



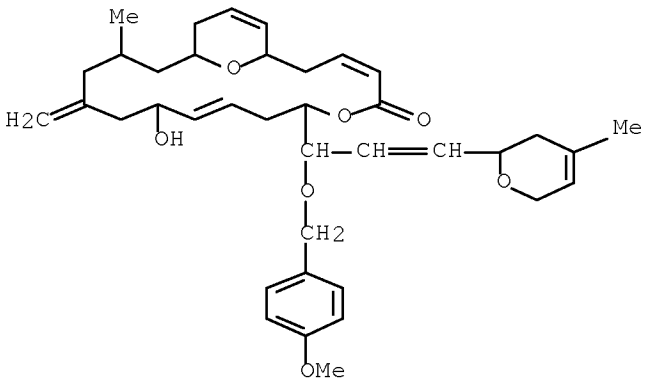
III

AB An enantioselective first total synthesis of laulimalide (I) is described. I, a remarkably potent antitumor macrolide, has been isolated from the Indonesian sponge Hyattella sp. and the Okinawan sponge Fasciospongia rimosa. I represents a new class of antitumor agents with significant clin. potential. The synthesis is convergent and involved the assembly of C3-C16 segment II and C17-C28 segment III by Julia olefination. The sensitive C2-C3 cis-olefin functionality was installed by Yamaguchi macrolactonization of a hydroxy alkynic acid followed by hydrogenation of the resulting alkynoic lactone over Lindlar's catalyst. Initial attempts of intramol. Still's variant of Horner-Emmons olefination between the C19-phosphonocetate and C3-aldehyde provided a 1:2 mixture of cis- and trans-macrolactones. The trans-isomer was photoisomerized to a mixture of cis- and trans-isomers. The other key steps involved ring-closing olefin metathesis to construct both dihydropyran units, stereoselective anomeric alkylation to functionalize the dihydropyran ring, stereoselective reduction of the resulting alkynyl ketone to set the C20-hydroxyl stereochem., and a novel Julia olefination protocol for the installation of the C13-exo-methylene unit. The sensitive epoxide at C16-C17 was introduced in a highly stereoselective manner by Sharpless epoxidn. at the final stage of the synthesis.

IT 312695-96-8P 385809-26-7P 385809-28-9P
725242-39-7P 725242-41-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(of macrolactone in total synthesis of (-)-laulimalide)

RN 312695-96-8 CAPLUS

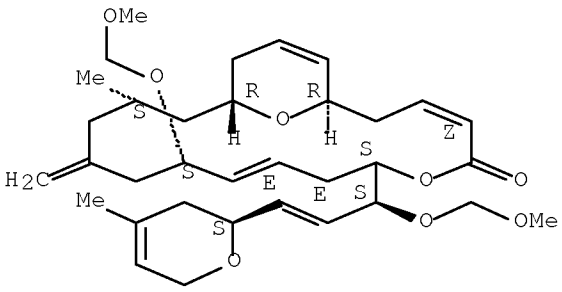
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(4-methoxyphenyl)methoxy]-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)



RN 385809-26-7 CAPLUS

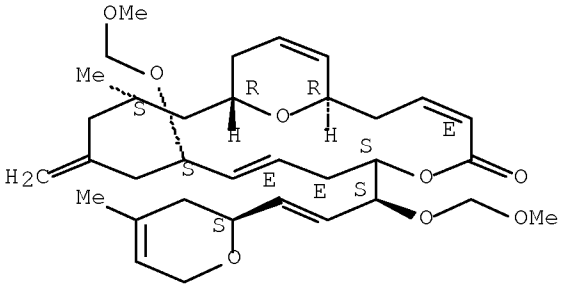
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



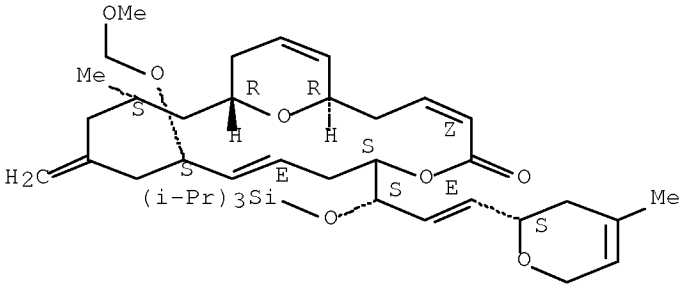
RN 385809-28-9 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3E,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 725242-39-7 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[tris(1-methylethyl)silyl]oxy]-2-propen-1-yl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

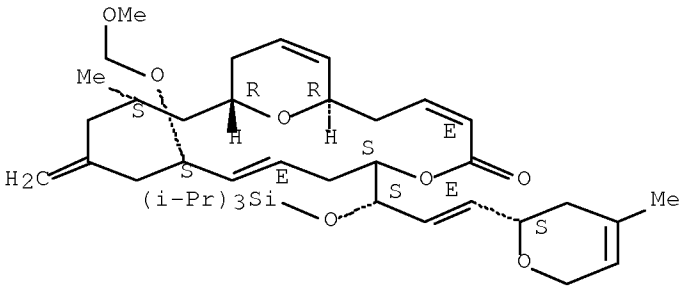
Absolute stereochemistry.
Double bond geometry as shown.



RN 725242-41-1 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[tris(1-methylethyl)silyl]oxy]-2-propen-1-yl]-11-(methoxymethoxy)-15-methyl-13-

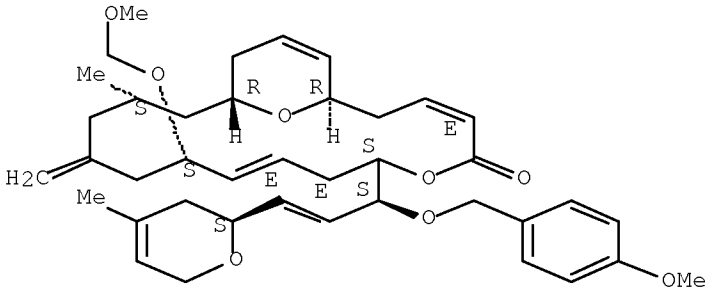
methylene-, (1R,3E,9E,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



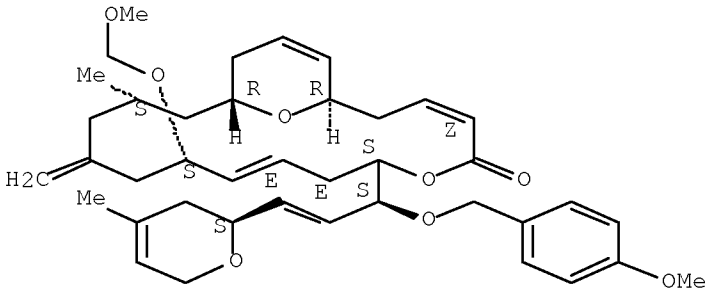
IT 312695-86-6P 312695-87-7P 312695-97-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (-)-laulimalide)
RN 312695-86-6 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(4-methoxyphenyl)methoxy]-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3E,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

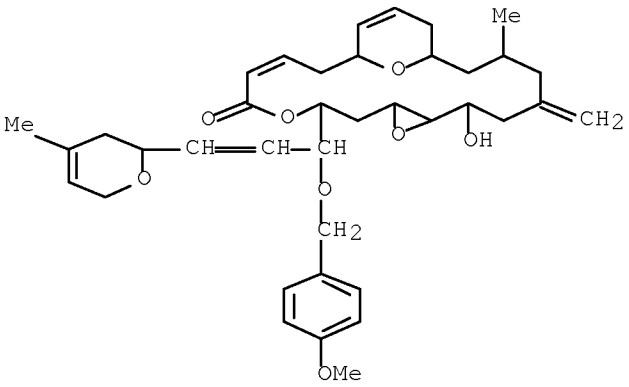


RN 312695-87-7 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(4-methoxyphenyl)methoxy]-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

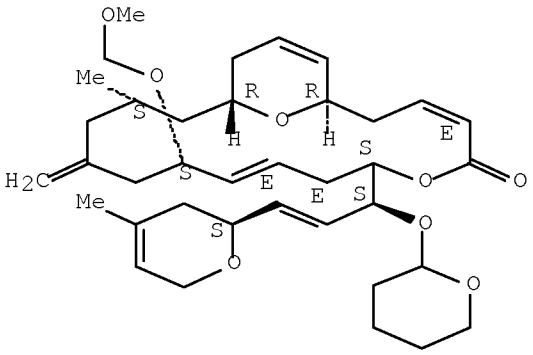


RN 312695-97-9 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(4-methoxyphenyl)methoxy]-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



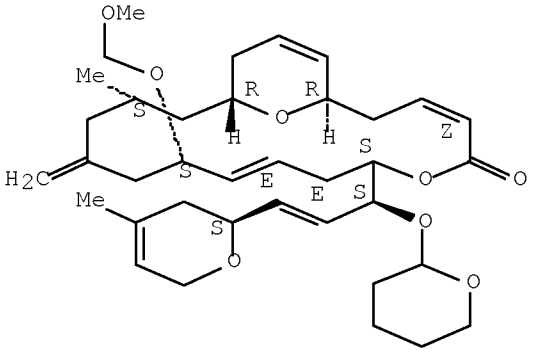
IT 349539-66-8P 394657-51-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of (-)-laulimalide)
RN 349539-66-8 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(tetrahydro-2H-pyran-2-yl)oxy]-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3E,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 394657-51-3 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(tetrahydro-2H-pyran-2-yl)oxy]-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:794451 CAPLUS Full-text
DOCUMENT NUMBER: 136:85720
TITLE: An intramolecular case of Sharpless kinetic resolution: total synthesis of laulimalide
AUTHOR(S): Mulzer, Johann; Ohler, Elisabeth
CORPORATE SOURCE: Institut fur Organische Chemie der Universitat Wien, Vienna, 1090, Austria
SOURCE: Angewandte Chemie, International Edition (2001), 40(20), 3842-3846
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:85720

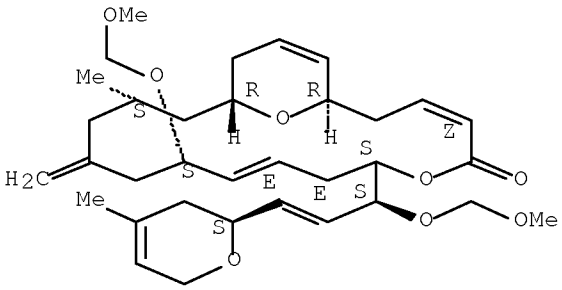
AB A convergent and stereocontrolled synthesis of laulimalide is described using Sharpless asym. epoxidn.

IT 385809-26-7 385809-28-9
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of laulimalide)

RN 385809-26-7 CAPLUS

CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

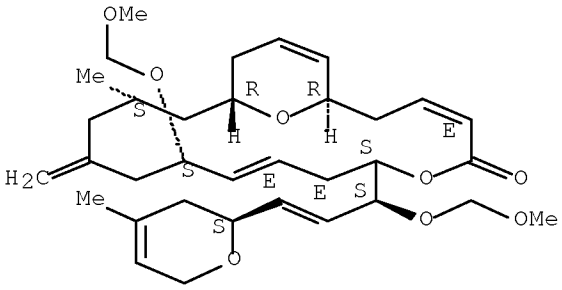
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 385809-28-9 CAPLUS

CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3E,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:733452 CAPLUS Full-text
DOCUMENT NUMBER: 136:19974
TITLE: Macrocyclization via allyl transfer: total synthesis of laulimalide
AUTHOR(S): Enev, Valentin S.; Kaehlig, Hanspeter; Mulzer, Johann
CORPORATE SOURCE: Institut fuer Organische Chemie, Universitat Wien, Vienna, A-1090, Austria

SOURCE: Journal of the American Chemical Society (2001), 123(43), 10764-10765
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:19974
GI

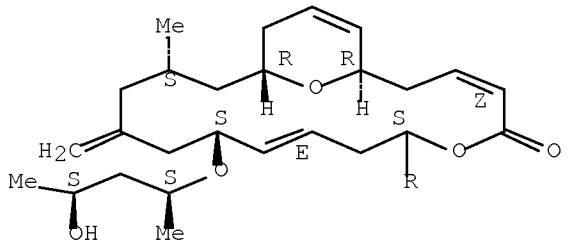
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

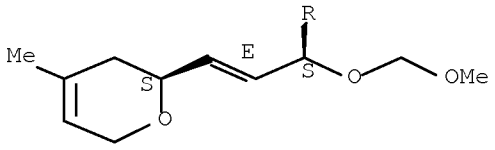
AB A stereocontrolled synthesis of the title compound I is described. The synthesis is highly convergent by assembling the mol. skeleton from two comparably sized fragments, phosphonate II and pyran aldehyde III, both of which are available from simple chiral starting materials. The longest linear sequence lists 19 steps with an overall yield of 21%. Novel features are the macrocyclization via competing allyl transfer type reactions and the orthogonality of two hydroxyl protecting groups, namely MOM and 4-oxopent-2-yl, resp.

IT 379269-82-6P 379269-83-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of laulimalide by macrocyclization via allyl transfer)

RN 379269-82-6 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propen-1-yl]-11-[(1S,3S)-3-hydroxy-1-methylbutoxy]-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

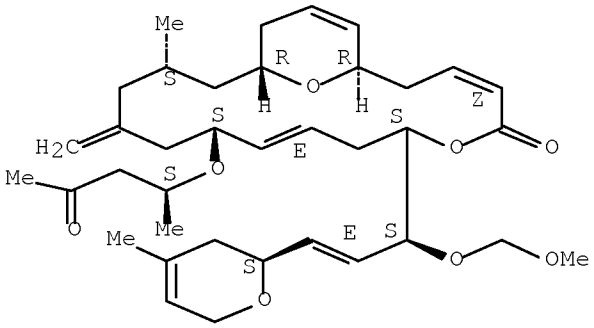




RN 379269-83-7 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-(methoxymethoxy)-2-propen-1-yl]-15-methyl-13-methylene-11-[(1S)-1-methyl-3-oxobutoxy]-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

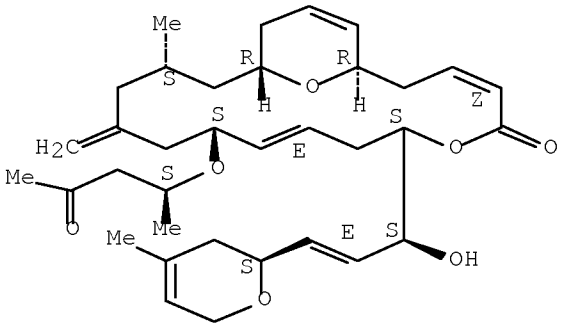
Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



IT 379269-88-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of laulimalide by macrocyclization via allyl transfer)
RN 379269-88-2 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propenyl]-15-methyl-13-methylene-11-[(1S)-1-methyl-3-oxobutoxy]-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:321112 CAPLUS Full-text
DOCUMENT NUMBER: 135:92475
TITLE: A macrolactonization-based strategy to obtain microtubule-stabilizing agent (-)-laulimalide
AUTHOR(S): Ghosh, A. K.; Wang, Y.
CORPORATE SOURCE: Department of Chemistry, University of Illinois at Chicago, Chicago, IL, 60607, USA
SOURCE: Tetrahedron Letters (2001), 42(20), 3399-3401
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:92475

AB An alternative synthesis of antitumor macrolide (-)-laulimalide is described. The synthesis was achieved utilizing Yamaguchi macrolactonization as the key step. The sensitive C2-C3 cis-olefin functionality has been installed by a macrolactonization of hydroxy alkynic acid and subsequent hydrogenation over Lindlar's catalyst.

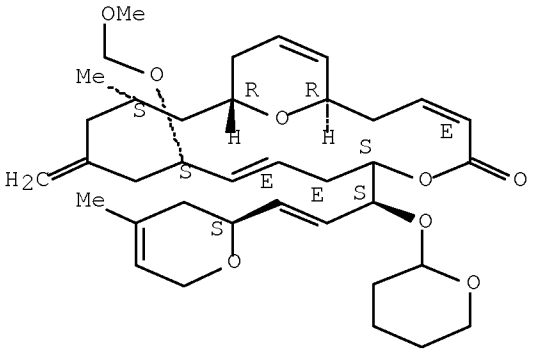
IT 349539-66-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 349539-66-8 CAPLUS

CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(tetrahydro-2H-pyran-2-yl)oxy]-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3E,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



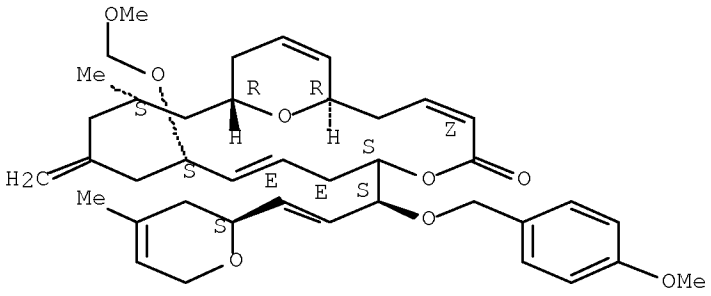
IT 312695-87-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective formal synthesis of (-)-laulimalide via a macrolactonization strategy)

RN 312695-87-7 CAPLUS

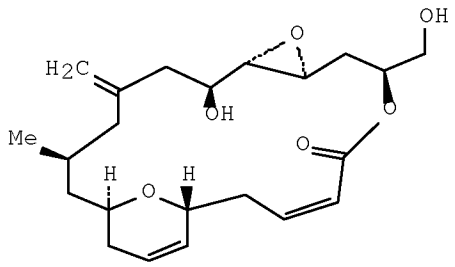
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(4-methoxyphenyl)methoxy]-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:908050 CAPLUS Full-text
DOCUMENT NUMBER: 134:193279
TITLE: Synthesis of the Macrocyclic Core of Laulimalide
AUTHOR(S): Paterson, Ian; de Savi, Chris; Tudge, Matthew
CORPORATE SOURCE: University Chemical Laboratory, Cambridge, CB2 1EW, UK
SOURCE: Organic Letters (2001), 3(2), 213-216
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:193279
GI



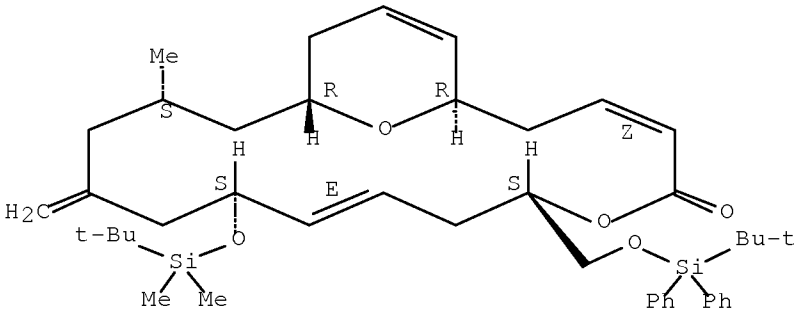
I

AB A stereoselective synthesis of I, corresponding to the fully functionalized macrocyclic core of the novel microtubule-stabilizing agent, laulimalide, has been completed. Efficient macrolactonization was achieved by a Mitsunobu reaction, installing the sensitive (Z)-enoate, and macrocyclic stereocontrol was then exploited to introduce the Me group and trans-epoxide.

IT 327027-84-9P 327027-85-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of the macrocyclic core of laulimalide)

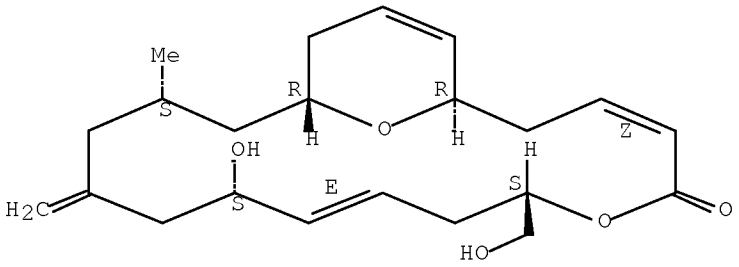
RN 327027-84-9 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 327027-85-0 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one,
11-hydroxy-7-(hydroxymethyl)-15-methyl-13-methylene-,
(1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

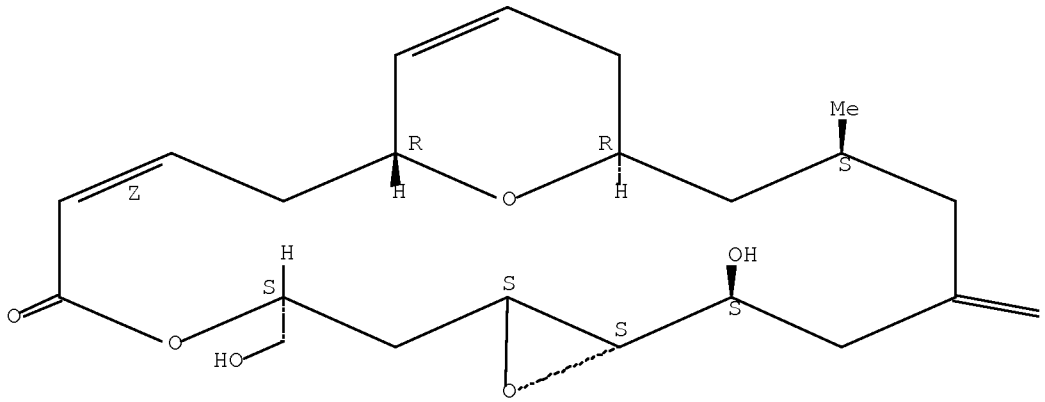
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT 327027-68-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of the macrocyclic core of laulimalide)
RN 327027-68-9 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one,
7-hydroxy-12-(hydroxymethyl)-3-methyl-5-methylene-,
(1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

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REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:742675 CAPLUS Full-text
DOCUMENT NUMBER: 134:42001
TITLE: Total Synthesis of (-)-Laulimalide
AUTHOR(S): Ghosh, Arun K.; Wang, Yong
CORPORATE SOURCE: Department of Chemistry, University of Illinois at Chicago, Chicago, IL, 60607, USA
SOURCE: Journal of the American Chemical Society (2000), 122(44), 11027-11028
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:42001
GI

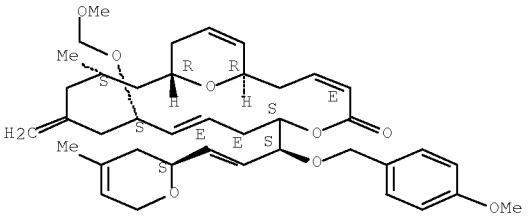
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

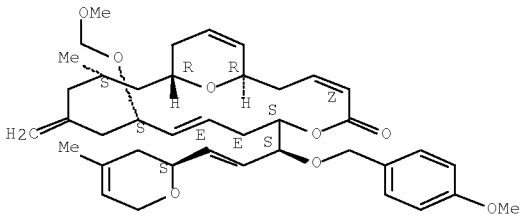
AB (-)-Laulimalidem (I) was prepared in a multistep synthesis via segments II and III.

IT 312695-86-6P 312695-87-7P 312695-96-8P
312695-97-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (-)-laulimalide)

RN 312695-86-6 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(4-methoxyphenyl)methoxy]-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3E,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

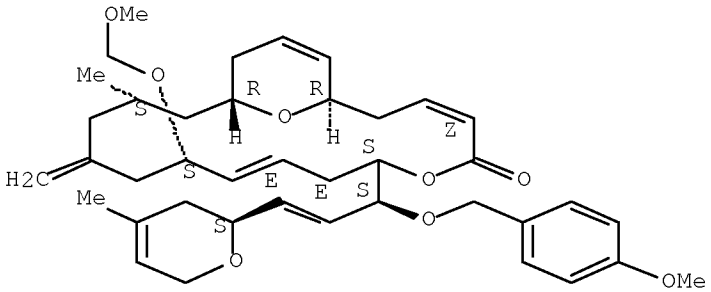
Absolute stereochemistry.
Double bond geometry as described by E or Z.



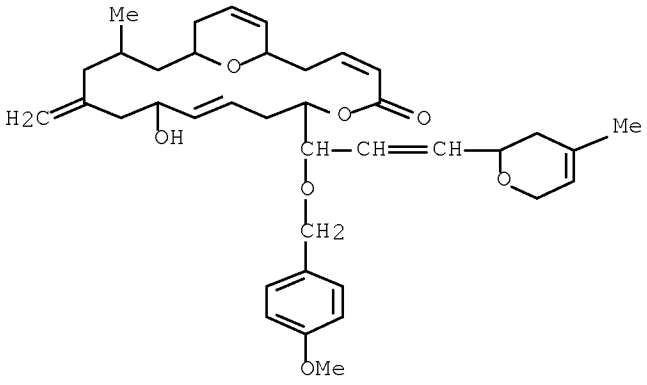


RN 312695-87-7 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(4-methoxyphenyl)methoxy]-2-propenyl]-11-(methoxymethoxy)-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)

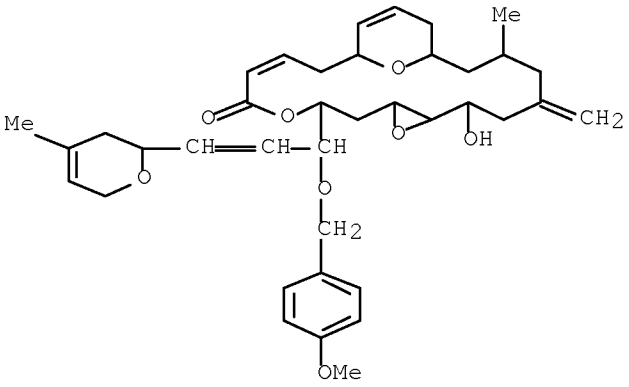
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 312695-96-8 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(4-methoxyphenyl)methoxy]-2-propenyl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (9CI) (CA INDEX NAME)



RN 312695-97-9 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[(4-methoxyphenyl)methoxy]-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



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DICTIONARY FILE UPDATES:   8 MAR 2009  HIGHEST RN 1117698-24-4

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L5             STR
L6             STR
L9           21 SEA FILE=REGISTRY SUB=L2 SSS FUL (L3 OR L4 OR L5 OR L6)
L27           1 SEA FILE=REGISTRY SPE=ON  ABB=ON  115268-43-4 THIS RN DEALT WITH
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FILE LAST UPDATED: 9 Mar 2009  (20090309/ED)
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L43  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2006:632688  CAPLUS  Full-text
DOCUMENT NUMBER:          145:262473
TITLE:                    Laulimalide and Synthetic Laulimalide Analogues are
                          Synergistic with Paclitaxel and 2-Methoxyestradiol
AUTHOR(S):                Clark, Erin A.; Hills, Patrice M.; Davidson, Bradley
                          S.; Wender, Paul A.; Mooberry, Susan L.
CORPORATE SOURCE:         Department of Physiology and Medicine, Southwest
                          Foundation for Biomedical Research, San Antonio, TX,
                          78227, USA
SOURCE:                   Molecular Pharmaceutics (2006), 3(4), 457-467
                          CODEN: MPOHBP; ISSN: 1543-8384
PUBLISHER:                American Chemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
```

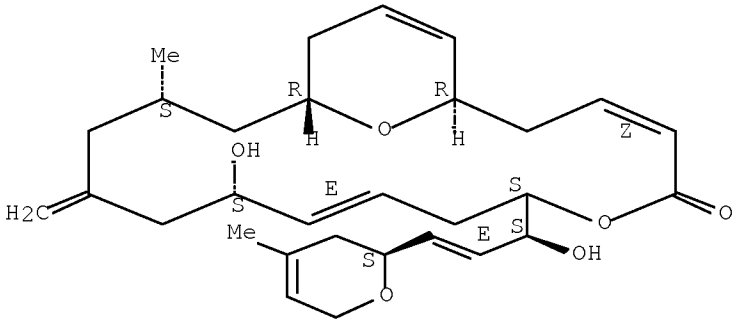
AB Some of the most significant therapeutic leads and agents used for the treatment of cancer target microtubule dynamics. Paclitaxel is an exceptional example that is currently used for treating a wide range of tumors. New, non-taxane microtubule stabilizers, including several epothilones, are advancing through clin. trials. Laulimalide is a potent microtubule stabilizer that binds to tubulin at a site that does not overlap the taxane-binding site. It is active against paclitaxel-resistant cancer cells. Notwithstanding its therapeutic potential, laulimalide is relatively unstable, rearranging to a more stable but less active isomer. The goal of this study was to evaluate the ability of laulimalide and two designed laulimalide analogs, C16-C17-des-epoxy laulimalide (LA1) and C20-methoxy laulimalide (LA2), to inhibit cell proliferation in combination with other tubulin-binding and non-tubulin-binding antiproliferative antimitotic agents. The synthetic laulimalide analogs retain the mechanism of action of the natural compound but do not share its instability. We studied the ability of the laulimalides to act

synergistically with paclitaxel, 2-methoxyestradiol, and monastrol, an Eg5 kinesin inhibitor. The results show that all three of the laulimalides acted synergistically with paclitaxel and 2-methoxyestradiol to inhibit proliferation with the analogs exhibiting significantly larger synergistic effects. The combination of laulimalide and monastrol was not synergistic and provided only additive effects. The laulimalide analogs LA1 and LA2 had a greater degree of synergy with both paclitaxel and 2-methoxyestradiol than was observed with laulimalide. Our results show that the laulimalides together with other tubulin-binding antimitotic agents provide synergistic antiproliferative actions. The data are consistent with the previously reported ability of laulimalide and paclitaxel to act synergistically to polymerize tubulin in vitro. These important findings suggest that specific combinations of microtubule-targeting agents should be considered for clin. utilities as they have excellent potential to improve clin. response.

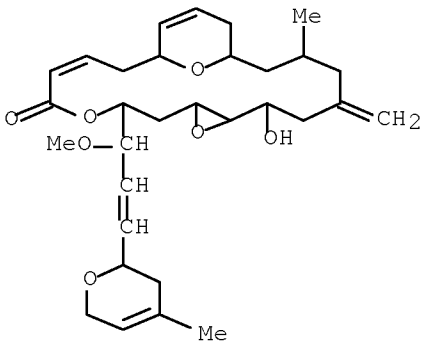
IT 352208-15-2, des-Epoxylaulimalide 352208-19-6, 20-O-Methyl-laulimalide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(laulimalide and synthetic laulimalide analogs are synergistic with paclitaxel and 2-methoxyestradiol)

RN 352208-15-2 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 352208-19-6 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



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L43 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:424258 CAPLUS Full-text
DOCUMENT NUMBER: 143:97200
TITLE: Total synthesis of (-)-laulimalide: Pd-catalyzed stereospecific ring construction of the substituted 3,6-dihydro[2H]pyran units
AUTHOR(S): Uenishi, Jun'ichi; Ohmi, Masashi
CORPORATE SOURCE: Kyoto Pharmaceutical University, Kyoto, 607-8412, Japan
SOURCE: Angewandte Chemie, International Edition (2005), 44(18), 2756-2760
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:97200
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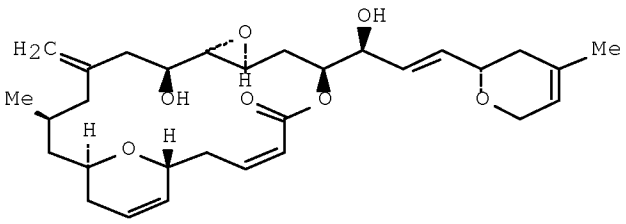


I

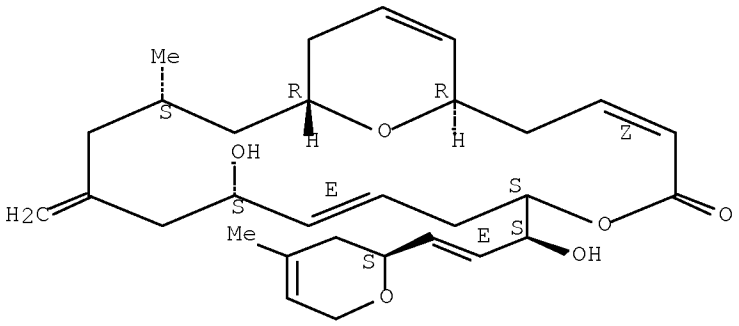
AB The potent anticancer agent (-)-laulimalide (I) was prepared through a versatile method that should allow access to other marine natural products. Key steps included a Pd-catalyzed 1,3 chirality transfer of an allylic alc. The syn-SN2'-like processes occur stereospecifically in either 6-endo-trig or 6-exo-trig fashion to give the desired 3,6-dihydro[2H]pyran rings.

IT 352208-15-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (-)-laulimalide via Pd-catalyzed stereospecific ring construction of the substituted 3,6-dihydro[2H]pyran units)

RN 352208-15-2 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one,

7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:516748 CAPLUS Full-text
DOCUMENT NUMBER: 141:184743
TITLE: Microtubule-stabilizing agents based on designed laulimalide analogues
AUTHOR(S): Mooberry, Susan L.; Randall-Hlubek, Deborah A.; Leal, Rachel M.; Hegde, Sayee G.; Hubbard, Robert D.; Zhang, Lei; Wender, Paul A.
CORPORATE SOURCE: Department of Physiology and Medicine, Southwest Foundation for Biomedical Research, San Antonio, TX, 78227, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2004), 101(23), 8803-8808
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

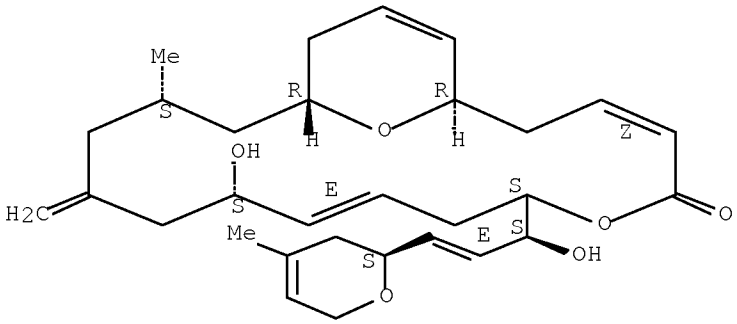
AB Laulimalide is a potent, structurally unique microtubule-stabilizing agent originally isolated from the marine sponge Cacospongia mycofijiensis. Laulimalide exhibits an activity profile different from other microtubule-binding agents, notably including effectiveness against paclitaxel-resistant cells, but it is intrinsically unstable. Five analogs of laulimalide were designed to exhibit enhanced chemical stability yet retain its exceptional biol. activities. Evaluations of these analogs showed that all are effective inhibitors of cancer-cell proliferation yet differ substantially in potency with an IC50 range of 0.12-16.5 μM. Although all of the analogs initiated cellular changes similar to laulimalide, including increased d. of interphase microtubules, aberrant mitotic spindles, and ultimately apoptosis, differences among the analogs were apparent. The two most potent analogs, C16-C17-des-epoxy laulimalide and C20-methoxy laulimalide, appear to have a mechanism of action identical to laulimalide. The C16-C17-des-epoxy, C20-methoxy laulimalide derivative, which incorporates both chemical changes of the most potent analogs, was significantly less potent and initiated the formation of unique interphase microtubules unlike the parent compound and other analogs. Two C2-C3-alkynoate derivs. had lower potency, and they initiated abnormal

microtubule structures but did not cause micronucleation or extensive G2/M accumulation. Significantly, paclitaxel- and epothilone-resistant cell lines were less resistant to the laulimalide analogs. In summary, analogs of laulimalide designed to minimize or eliminate its intrinsic instability have been synthesized, and some have been found to retain the unique biol. activities of laulimalide.

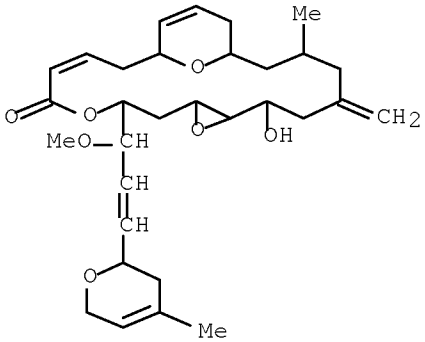
IT 352208-15-2 352208-19-6 449180-74-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(laulimalide analogs as microtubule-stabilizing agents)

RN 352208-15-2 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



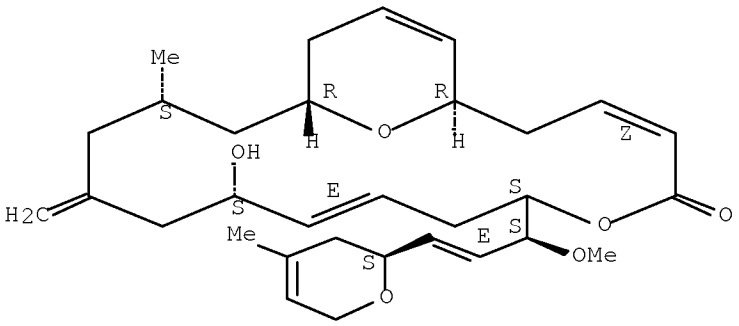
RN 352208-19-6 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)-(9CI) (CA INDEX NAME)



RN 449180-74-9 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propen-1-yl]-11-hydroxy-15-methyl-13-methylene-, (1R,7S,11S,15S,17R)- (CA INDEX

NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:473227 CAPLUS Full-text
DOCUMENT NUMBER: 137:179522
TITLE: The Microtubule Stabilizing Agent Laulimalide Does Not Bind in the Taxoid Site, Kills Cells Resistant to Paclitaxel and Epothilones, and May Not Require Its Epoxide Moiety for Activity
AUTHOR(S): Pryor, Donald E.; O'Brate, Aurora; Bilcer, Geoffrey; Diaz, J. Fernando; Wang, Yuefang; Wang, Yong; Kabaki, Mikio; Jung, M. Katherine; Andreu, Jose M.; Ghosh, Arun K.; Giannakakou, Paraskevi; Hamel, Ernest
CORPORATE SOURCE: Screening Technologies Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute at Frederick, National Institutes of Health, Frederick, MD, 21702, USA
SOURCE: Biochemistry (2002), 41(29), 9109-9115
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Laulimalide is a cytotoxic natural product that stabilizes microtubules. The compound enhances tubulin assembly, and laulimalide is quant. comparable to paclitaxel in its effects on the reaction. Laulimalide is also active in P-glycoprotein overexpressing cells, while isolaulimalide, a congener without the drug's epoxide moiety, was reported to have negligible cytotoxic and biochem. activity [Mooberry et al. (1999) Cancer Res. 59, 653-660]. The authors report here that laulimalide binds at a site on tubulin polymer that is distinct from the taxoid site. The authors found that laulimalide, while as active as paclitaxel, epothilone A, and eleutherobin in promoting the assembly of cold-stable microtubules, was unable to inhibit the binding of radiolabeled paclitaxel or of 7-O-[N-(2,7-difluoro-4'-fluoresceincarbonyl)-L-alanyl]paclitaxel, a fluorescent paclitaxel derivative, to tubulin. Confirming this observation, the authors demonstrated that microtubules formed in the presence of both laulimalide and paclitaxel contained near-molar quantities, relative to tubulin, of both drugs. Laulimalide was active against human ovarian carcinoma cell lines resistant to paclitaxel or

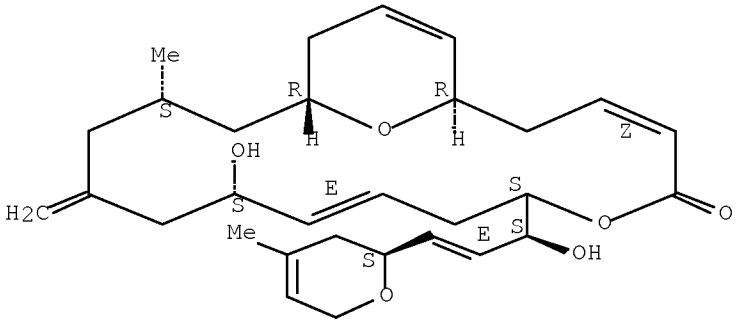
epothilones A and B on the basis of mutations in the M40 human β-tubulin gene. The authors also report that a laulimalide analog lacking the epoxide moiety, while less active than laulimalide in biochem. and cellular systems, is probably more active than isolaulimalide. Further exploration of the role of the epoxide in the interaction of laulimalide with tubulin is therefore justified.

IT 352208-15-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microtubule stabilizing agent laulimalide does not bind in taxoid site and kills tumor cells resistant to paclitaxel and epothilones and may not require epoxide moiety for activity)

RN 352208-15-2 CAPLUS

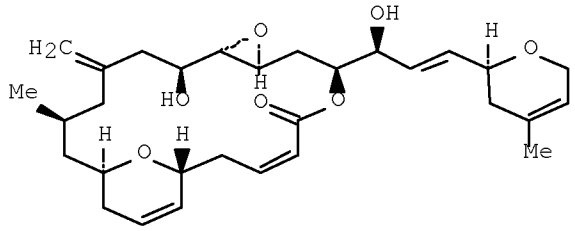
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

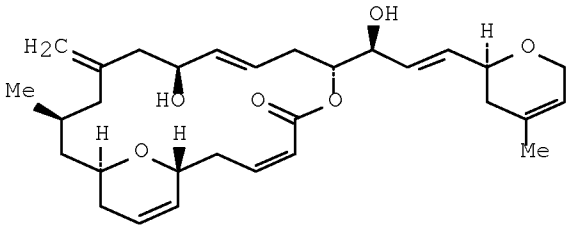


REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:650750 CAPLUS Full-text
DOCUMENT NUMBER: 135:371556
TITLE: Total Synthesis of the Microtubule-Stabilizing Agent (-)-Laulimalide
AUTHOR(S): Paterson, Ian; De Savi, Chris; Tudge, Matthew
CORPORATE SOURCE: University Chemical Laboratory, Cambridge, CB2 1EW, UK
SOURCE: Organic Letters (2001), 3(20), 3149-3152
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:371556
GI



I



II

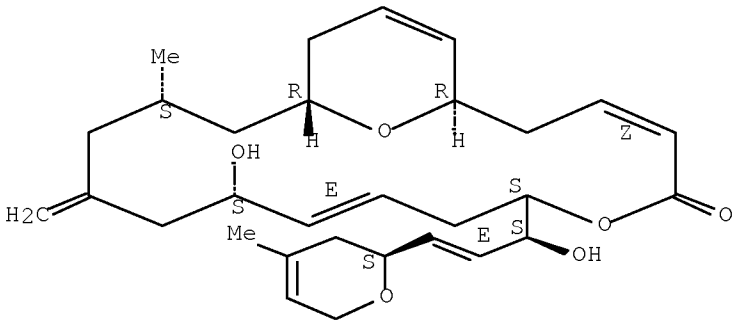
AB The total synthesis of the potent microtubule-stabilizing anticancer agent (-)-laulimalide (I) has been achieved in 27 steps and 2.9% overall yield. Notable features are the use of Jacobsen HDA chemical for the enantioselective construction of the side chain dihydropyran, a diastereoselective aldol coupling using chiral boron enolate methodol., a Mitsunobu macrolactonization, and a Sharpless AE to introduce the epoxide onto des-epoxy-laulimalide (II).

IT 352208-15-2P, des-Epoxylaulimalide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of the microtubule-stabilizing agent (-)-laulimalide)

RN 352208-15-2 CAPLUS

CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:564831 CAPLUS Full-text

DOCUMENT NUMBER: 135:132428
TITLE: Laulimalide compounds as microtubule stabilizing agents, and use in the inhibition of cell proliferation
INVENTOR(S): Mooberry, Susan L.; Davidson, Bradley S.
PATENT ASSIGNEE(S): University of Hawaii, USA; Utah State University
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054689	A1	20010802	WO 2001-US2590	20010126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6414015	B1	20020702	US 2000-493897	20000128
US 20020198256	A1	20021226	US 2002-126674	20020419
US 7435754	B2	20081014		

PRIORITY APPLN. INFO.: US 2000-493897 A1 20000128
WO 2001-US2590 W 20010126

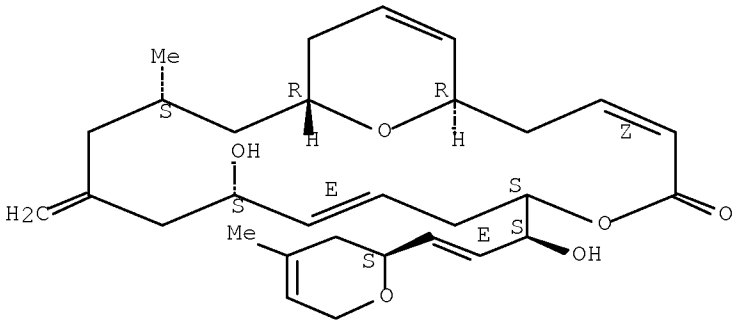
OTHER SOURCE(S): MARPAT 135:132428

AB Methods are disclosed for inhibiting the proliferation of hyperproliferative mammalian cells having a multiple drug-resistant phenotype using an amount of a laulimalide compound effective to disrupt the dynamic state of microtubule polymerization and depolymn. to arrest cell mitosis, as are laulimalide compds., and compns. containing them, which find use in the methods.

IT 352208-15-2D, derivs. 352208-16-3 352208-17-4 352208-18-5 352208-19-6 352208-20-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(laulimalide compds. as microtubule stabilizing agents, and use in inhibition of cell proliferation)

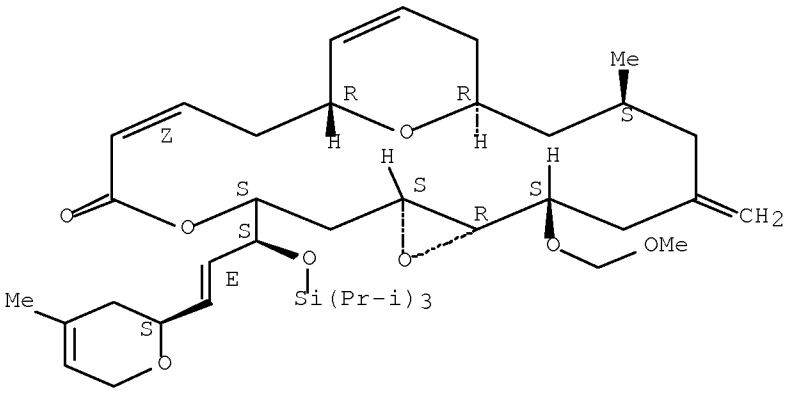
RN 352208-15-2 CAPLUS
CN 6,21-Dioxabicyclo[15.3.1]heneicosa-3,9,19-trien-5-one, 7-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-1-yl]-11-hydroxy-15-methyl-13-methylene-, (1R,3Z,7S,9E,11S,15S,17R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

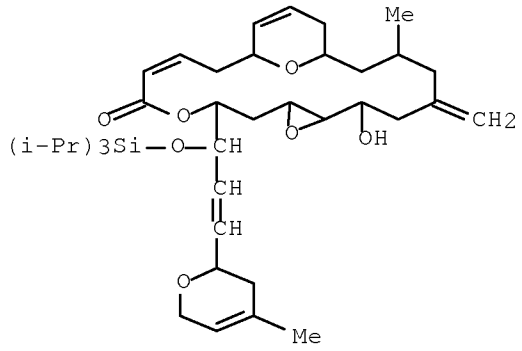


RN 352208-16-3 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[tris(1-methylethyl)silyl]oxy]-2-propenyl]-7-(methoxymethoxy)-3-methyl-5-methylene-, (1R,3S,7S,8R,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

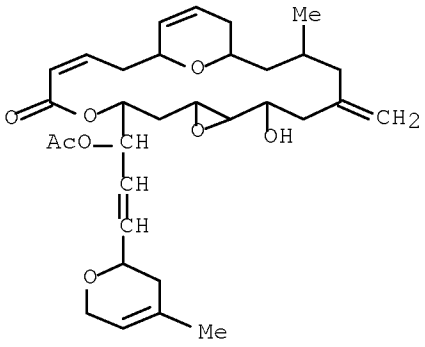
Absolute stereochemistry.
Double bond geometry as shown.



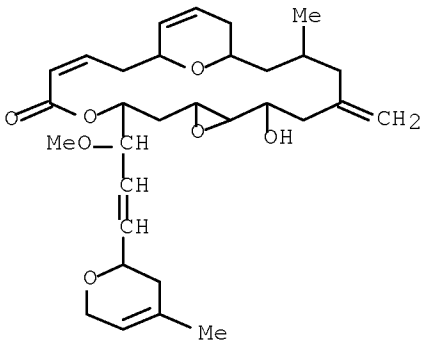
RN 352208-17-4 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-[[tris(1-methylethyl)silyl]oxy]-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)



RN 352208-18-5 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-1-(acetyloxy)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)-(9CI) (CA INDEX NAME)



RN 352208-19-6 CAPLUS
CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-methoxy-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)-(9CI) (CA INDEX NAME)

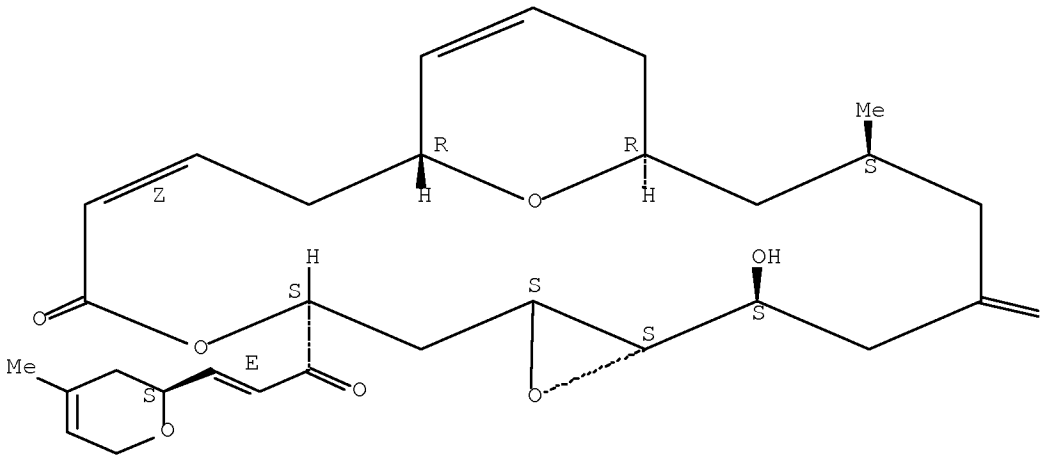


RN 352208-20-9 CAPLUS

CN 9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one, 12-[(2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-oxo-2-propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s l38 and l40
L44         13 L38 AND L40    OVERLAP BETWEEN STRUCTURE SEARCH PARTS 1 & 2;
                              THESE REFERENCES WERE PRINTED IN FULL BEGINNING
                              ON p. 34
=> d scan ti

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   A de Novo Enantioselective Total Synthesis of (-)-Laulimalide

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):13

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Preparation of laulimalide and its derivatives for pharmaceutical uses

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Preparation of laulimalide and epothilone derivatives as microtubule
     stabilizing compounds

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Sponge-Derived Fijianolide Polyketide Class: Further Evaluation of Their
     Structural and Cytotoxicity Properties

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Macrocyclization via allyl transfer: total synthesis of laulimalide

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Total Synthesis of (-)-Laulimalide

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Preparation of laulimalide derivatives for treating diseases of cellular
     hyperproliferation

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Total Synthesis of the Microtubule Stabilizing Antitumor Agent Laulimalide
     and Some Nonnatural Analogues: The Power of Sharpless' Asymmetric
     Epoxidation

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Synthesis and Biological Evaluation of (-)-Laulimalide Analogues

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   3-D QSAR studies of microtubule stabilizing antimitotic agents towards six
     cancer cell lines

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Processes for the synthesis of laulimalide and its analogs and methods for
     the treatment of proliferative disease

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   An intramolecular case of Sharpless kinetic resolution: total synthesis of
     laulimalide

L44   13 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Total synthesis of the antitumor agent (-)-laulimalide

ALL ANSWERS HAVE BEEN SCANNED
```

STRUCTURE SEARCH PART 3

```
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DICTIONARY FILE UPDATES:   8 MAR 2009  HIGHEST RN 1117698-24-4

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http://www.cas.org/support/stngen/stndoc/properties.html


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     12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-propen-
     1-yl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)-  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one,
     12-[(1S,2E)-3-[(2S)-3,6-dihydro-4-methyl-2H-pyran-2-yl]-1-hydroxy-2-
     propenyl]-7-hydroxy-3-methyl-5-methylene-, (1R,3S,7S,8S,10S,12S,15Z,18R)-
     (9CI)
CN   9,13,22-Trioxatricyclo[16.3.1.08,10]docosa-15,19-dien-14-one,
     12-[3-(3,6-dihydro-4-methyl-2H-pyran-2-yl)-1-hydroxy-2-propenyl]-7-hydroxy-
     3-methyl-5-methylene-, [1R-
     [1R*,3S*,7S*,8S*,10S*,12S*[1S*,2E,3(S*)],15Z,18R*]]-
OTHER NAMES:
CN   (-)-Laulimalide
CN   ER 806782
CN   Fijianolide B
CN   Laulimalide
FS   STEREOSEARCH
DR   114995-73-2
MF   C30 H42 O7
SR   CA
LC   STN Files:   ADISNEWS, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS,
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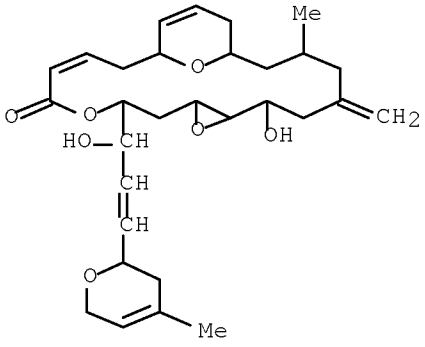
CASREACT, DDFU, DRUGU, EMBASE, NAPRALERT, RTECS*, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

120 REFERENCES IN FILE CA (1907 TO DATE)
14 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
123 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil capl; d que nos l30
FILE 'CAPLUS' ENTERED AT 09:24:23 ON 10 MAR 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 10 Mar 2009 VOL 150 ISS 11
FILE LAST UPDATED: 9 Mar 2009 (20090309/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

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This file contains CAS Registry Numbers for easy and accurate substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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L27           1 SEA FILE=REGISTRY SPE=ON  ABB=ON  115268-43-4
L30         123 SEA FILE=CAPLUS SPE=ON  ABB=ON  L27

=> d py l30 123

L30  ANSWER 123 OF 123  CAPLUS  COPYRIGHT 2009 ACS on STN
PY   1988         PUBLICATION YEAR OF OLDEST REFERENCE CONTAINING THIS RN

=> s l30 and l40,l38
L45         25 L30 AND (L40 OR L38)       REFERENCES PREVIOUSLY DISPLAYED THAT
                                          CONTAINED THIS RN

=> d scan ti

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Synthesis of (-)-laulimalide: an agent for microtubule stabilization

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):25

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Synthesis and biological evaluation of (-)-laulimalide analogues

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   A macrolactonization-based strategy to obtain microtubule-stabilizing
     agent (-)-laulimalide

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Asymmetric Total Synthesis of (-)-Laulimalide: Exploiting the Asymmetric
     Glycolate Alkylation Reaction

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Preparation of laulimalide and epothilone derivatives as microtubule
     stabilizing compounds

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Synthesis of the Macrocyclic Core of Laulimalide

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Total synthesis of the antitumor agent (-)-laulimalide

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Synthesis and Biological Evaluation of (-)-Laulimalide Analogues

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Total Synthesis of (-)-Laulimalide

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Total Synthesis of (-)-Laulimalide

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Preparation of laulimalide and its derivatives for pharmaceutical uses

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Processes for the synthesis of laulimalide and its analogs and methods for
     the treatment of proliferative disease

L45   25 ANSWERS   CAPLUS  COPYRIGHT 2009 ACS on STN
TI   Total Synthesis of Microtubule-Stabilizing Agent (-)-Laulimalide
```

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI Total Synthesis of the Microtubule Stabilizing Antitumor Agent Laulimalide and Some Nonnatural Analogues: The Power of Sharpless' Asymmetric Epoxidation

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI Sponge-Derived Fijianolide Polyketide Class: Further Evaluation of Their Structural and Cytotoxicity Properties

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI An intramolecular case of Sharpless kinetic resolution: total synthesis of laulimalide

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI A de Novo Enantioselective Total Synthesis of (-)-Laulimalide

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI Laulimalide and Synthetic Laulimalide Analogues are Synergistic with Paclitaxel and 2-Methoxyestradiol

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI Macrocyclization via allyl transfer: total synthesis of laulimalide

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI Preparation of laulimalide derivatives for treating diseases of cellular hyperproliferation

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI Total synthesis of (-)-laulimalide: Pd-catalyzed stereospecific ring construction of the substituted 3,6-dihydro[2H]pyran units

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI Total Synthesis of the Microtubule-Stabilizing Agent (-)-Laulimalide

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI The Microtubule Stabilizing Agent Laulimalide Does Not Bind in the Taxoid Site, Kills Cells Resistant to Paclitaxel and Epothilones, and May Not Require Its Epoxide Moiety for Activity

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI Preparation of laulimalide analogs for use in pharmaceutical compositions as chemotherapeutic, antiproliferative, anticancer agents

L45 25 ANSWERS CAPLUS COPYRIGHT 2009 ACS on STN
TI Laulimalide compounds as microtubule stabilizing agents, and use in the inhibition of cell proliferation

ALL ANSWERS HAVE BEEN SCANNED

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FILE 'HOME' ENTERED AT 09:25:48 ON 10 MAR 2009

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=> d stat que l10; d his nofile
L1              STR
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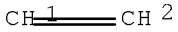

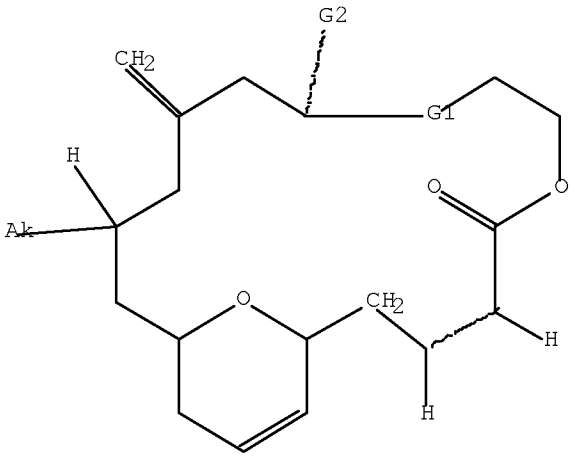

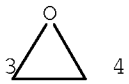


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G1 [@1-@2],[@3-@4]
G2 O,N
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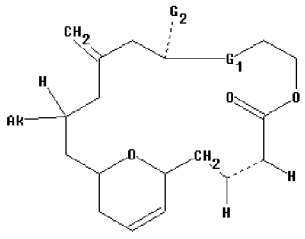
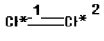
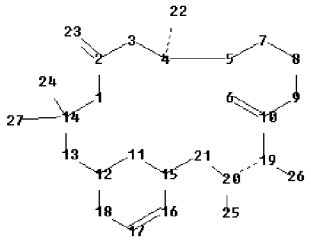
Structure attributes must be viewed using STN Express query preparation.

Uploading L1.str








```
chain nodes :
6  22  23  24  25  26  27  28  29
ring nodes :
1  2  3  4  5  7  8  9  10  11  12  13  14  15  16  17  18  19  20  21  30  31  32
```

chain bonds :
2-23 4-22 6-10 14-24 14-27 19-26 20-25 28-29
ring bonds :
1-14 1-2 2-3 3-4 4-5 5-7 7-8 8-9 9-10 10-19 11-15 11-12 12-13 12-18
13-14 15-16 15-21 16-17 17-18 19-20 20-21 30-31 30-32 31-32
exact/norm bonds :
1-14 1-2 2-3 2-23 3-4 4-5 4-22 5-7 6-10 7-8 8-9 9-10 10-19 11-15 11-
12 12-13 12-18 13-14 14-24 14-27 15-16 15-21 16-17 17-18 19-20 19-26
20-21 20-25 28-29 30-31 30-32 31-32

G1:[*1-*2],[*3-*4]

G2:O,N

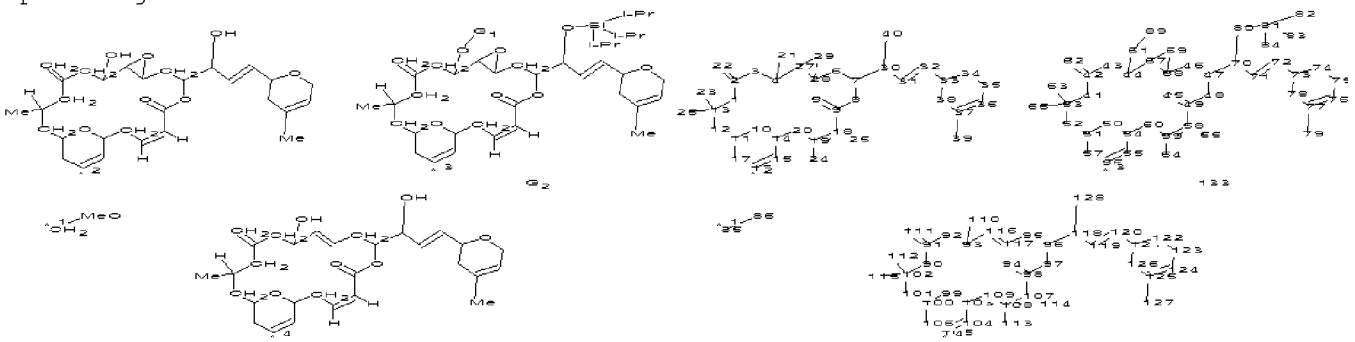
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS 29:CLASS 30:Atom 31:Atom 32:Atom

L2 119 SEA FILE=REGISTRY SSS FUL L1
L3 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

Uploading L3.str



chain nodes :
5 21 22 23 24 25 26 30 31 32 39 40 45 61 62 63 64 65 66 70 71
72 79 80 81 82 83 84 85 86 89 94 110 111 112 113 114 115 118 119
120 127 128 133
ring nodes :
1 2 3 4 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 27 28 29 33
34 35 36 37 38 41 42 43 44 46 47 48 49 50 51 52 53 54 55 56 57
58 59 60 67 68 69 73 74 75 76 77 78 90 91 92 93 95 96 97 98 99
100 101 102 103 104 105 106 107 108 109 116 117 121 122 123 124 125
126
chain bonds :
2-22 4-21 5-9 7-30 13-23 13-26 18-25 19-24 30-31 30-40 31-32 32-33 37-
39 42-62 44-61 45-49 47-70 53-63 53-66 58-65 59-64 61-89 70-71 70-80
71-72 72-73 77-79 80-81 81-82 81-83 81-84 85-86 91-111 93-110 94-98 96-
118 102-112 102-115 107-114 108-113 118-119 118-128 119-120 120-121 125-
127

ring bonds :
1-13 1-2 2-3 3-4 4-27 6-7 6-28 7-8 8-9 9-18 10-14 10-11 11-12 11-17
12-13 14-15 14-20 15-16 16-17 18-19 19-20 27-28 27-29 28-29 33-34 33-38
34-35 35-36 36-37 37-38 41-53 41-42 42-43 43-44 44-67 46-47 46-68 47-48
48-49 49-58 50-54 50-51 51-52 51-57 52-53 54-55 54-60 55-56 56-57 58-59
59-60 67-68 67-69 68-69 73-74 73-78 74-75 75-76 76-77 77-78 90-102 90-91
91-92 92-93 93-116 95-96 95-117 96-97 97-98 98-107 99-103 99-100 100-101
100-106 101-102 103-104 103-109 104-105 105-106 107-108 108-109 116-117
121-122 121-126 122-123 123-124 124-125 125-126
exact/norm bonds :
1-13 1-2 2-3 3-4 4-21 4-27 5-9 6-7 6-28 7-8 8-9 9-18 10-14 10-11 11-
12 11-17 12-13 14-15 14-20 15-16 16-17 18-19 19-20 27-28 27-29 28-29
30-40 33-34 33-38 34-35 35-36 36-37 37-38 41-53 41-42 42-43 43-44 44-61
44-67 45-49 46-47 46-68 47-48 48-49 49-58 50-54 50-51 51-52 51-57 52-53
54-55 54-60 55-56 56-57 58-59 59-60 61-89 67-68 67-69 68-69 70-80 73-74
73-78 74-75 75-76 76-77 77-78 90-102 90-91 91-92 92-93 93-110 93-116 94-
98 95-96 95-117 96-97 97-98 98-107 99-103 99-100 100-101 100-106 101-102
103-104 103-109 104-105 105-106 107-108 108-109 116-117 118-128 121-122
121-126 122-123 123-124 124-125 125-126
exact bonds :
2-22 7-30 13-23 13-26 18-25 19-24 30-31 31-32 32-33 37-39 42-62 47-70
53-63 53-66 58-65 59-64 70-71 71-72 72-73 77-79 80-81 81-82 81-83 81-84
85-86 91-111 96-118 102-112 102-115 107-114 108-113 118-119 119-120 120-
121 125-127

G1:H,[*1]

G2:[*2],[*3],[*4]

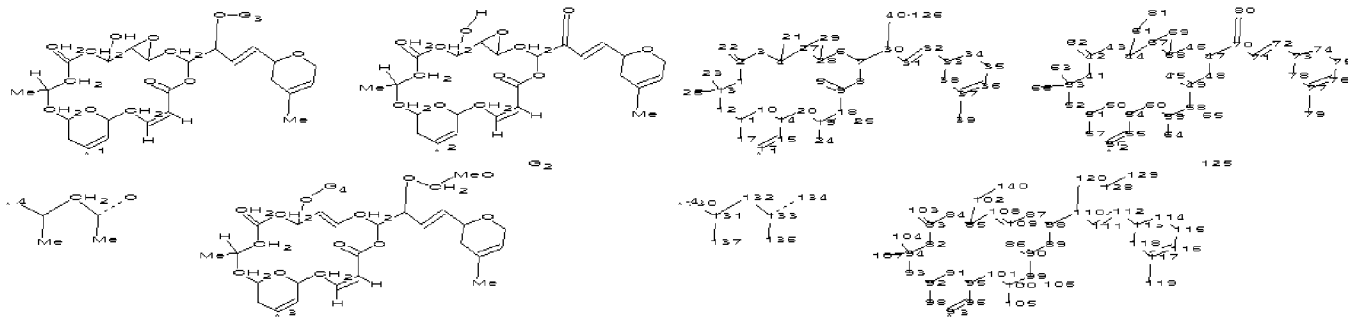
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:CLASS 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:Atom
28:Atom 29:Atom 30:CLASS 31:CLASS 32:CLASS 33:Atom 34:CLASS 35:CLASS
36:CLASS 37:Atom 38:Atom 39:CLASS 40:CLASS 41:Atom 42:Atom 43:Atom 44:Atom
45:CLASS 46:Atom 47:Atom 48:Atom 49:Atom 50:Atom 51:Atom 52:Atom 53:Atom
54:Atom 55:Atom 56:Atom 57:Atom 58:Atom 59:Atom 60:Atom 61:CLASS 62:CLASS
63:CLASS 64:CLASS 65:CLASS 66:CLASS 67:Atom 68:Atom 69:Atom 70:CLASS
71:CLASS 72:CLASS 73:Atom 74:CLASS 75:CLASS 76:CLASS 77:Atom 78:Atom
79:CLASS 80:CLASS 81:CLASS 82:CLASS 83:CLASS 84:CLASS 85:CLASS 86:CLASS
89:CLASS 90:Atom 91:Atom 92:Atom 93:Atom 94:CLASS 95:Atom 96:Atom 97:Atom
98:Atom 99:Atom 100:Atom 101:Atom 102:Atom 103:Atom 104:Atom 105:Atom
106:Atom 107:Atom 108:Atom 109:Atom 110:CLASS 111:CLASS 112:CLASS 113:CLASS
114:CLASS 115:CLASS 116:Atom 117:Atom 118:CLASS 119:CLASS 120:CLASS 121:Atom
122:CLASS 123:CLASS 124:CLASS 125:Atom 126:Atom 127:CLASS 128:CLASS
133:CLASS

L4 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

Uploading L4.str



chain nodes :
5 21 22 23 24 25 26 30 31 32 39 40 45 61 62 63 64 65 66 70 71
72 79 80 81 86 102 103 104 105 106 107 110 111 112 119 120 125 126
128 129 130 131 132 133 134 136 137 140
ring nodes :
1 2 3 4 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 27 28 29 33
34 35 36 37 38 41 42 43 44 46 47 48 49 50 51 52 53 54 55 56 57
58 59 60 67 68 69 73 74 75 76 77 78 82 83 84 85 87 88 89 90 91
92 93 94 95 96 97 98 99 100 101 108 109 113 114 115 116 117 118
chain bonds :
2-22 4-21 5-9 7-30 13-23 13-26 18-25 19-24 30-31 30-40 31-32 32-33 37-
39 40-126 42-62 44-61 45-49 47-70 53-63 53-66 58-65 59-64 61-81 70-71
70-80 71-72 72-73 77-79 83-103 85-102 86-90 88-110 94-104 94-107 99-106
100-105 102-140 110-111 110-120 111-112 112-113 117-119 120-128 128-129
130-131 131-132 131-137 132-133 133-134 133-136
ring bonds :
1-13 1-2 2-3 3-4 4-27 6-7 6-28 7-8 8-9 9-18 10-14 10-11 11-12 11-17
12-13 14-15 14-20 15-16 16-17 18-19 19-20 27-28 27-29 28-29 33-34 33-38
34-35 35-36 36-37 37-38 41-53 41-42 42-43 43-44 44-67 46-47 46-68 47-48
48-49 49-58 50-54 50-51 51-52 51-57 52-53 54-55 54-60 55-56 56-57 58-59
59-60 67-68 67-69 68-69 73-74 73-78 74-75 75-76 76-77 77-78 82-94 82-83
83-84 84-85 85-108 87-88 87-109 88-89 89-90 90-99 91-95 91-92 92-93 92-
98 93-94 95-96 95-101 96-97 97-98 99-100 100-101 108-109 113-114 113-118
114-115 115-116 116-117 117-118
exact/norm bonds :
1-13 1-2 2-3 3-4 4-21 4-27 5-9 6-7 6-28 7-8 8-9 9-18 10-14 10-11 11-
12 11-17 12-13 14-15 14-20 15-16 16-17 18-19 19-20 27-28 27-29 28-29
30-40 33-34 33-38 34-35 35-36 36-37 37-38 40-126 41-53 41-42 42-43 43-44
44-61 44-67 45-49 46-47 46-68 47-48 48-49 49-58 50-54 50-51 51-52 51-57
52-53 54-55 54-60 55-56 56-57 58-59 59-60 67-68 67-69 68-69 70-80 73-74
73-78 74-75 75-76 76-77 77-78 82-94 82-83 83-84 84-85 85-102 85-108 86-
90 87-88 87-109 88-89 89-90 90-99 91-95 91-92 92-93 92-98 93-94 95-96
95-101 96-97 97-98 99-100 100-101 102-140 108-109 110-120 113-114 113-118
114-115 115-116 116-117 117-118 133-134
exact bonds :
2-22 7-30 13-23 13-26 18-25 19-24 30-31 31-32 32-33 37-39 42-62 47-70
53-63 53-66 58-65 59-64 61-81 70-71 71-72 72-73 77-79 83-103 88-110 94-
104 94-107 99-106 100-105 110-111 111-112 112-113 117-119 120-128 128-129
130-131 131-132 131-137 132-133 133-136

G2:[*1],[*2],[*3]

G3:CH3,C(O)CH3

G4:H,[*4]

Connectivity :

134:1 E exact RC ring/chain
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:CLASS 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
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28:Atom 29:Atom 30:CLASS 31:CLASS 32:CLASS 33:Atom 34:CLASS 35:CLASS
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132:CLASS 133:CLASS 134:CLASS 136:CLASS 137:CLASS 140:CLASS

L5 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

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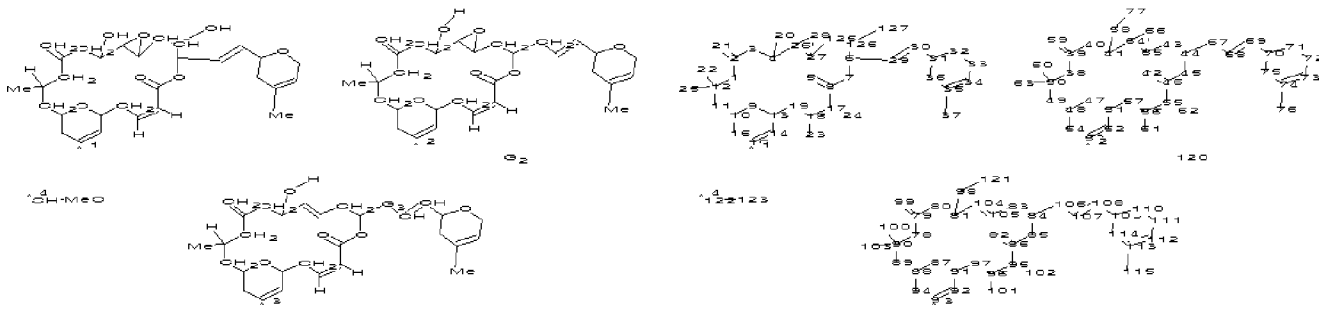

chain nodes :
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77 82 98 99 100 101 102 103 106 107 108 115 120 121 122 123 127
ring nodes :
1 2 3 4 6 7 8 9 10 11 12 13 14 15 16 17 18 19 26 27 28 31 32
33 34 35 36 38 39 40 41 43 44 45 46 47 48 49 50 51 52 53 54 55
56 57 64 65 66 70 71 72 73 74 75 78 79 80 81 83 84 85 86 87 88
89 90 91 92 93 94 95 96 97 104 105 109 110 111 112 113 114 125
126
chain bonds :
2-21 4-20 5-8 6-29 12-22 12-25 17-24 18-23 29-30 30-31 35-37 39-59 41-
58 42-46 44-67 50-60 50-63 55-62 56-61 58-77 67-68 68-69 69-70 74-76
79-99 81-98 82-86 84-106 90-100 90-103 95-102 96-101 98-121 106-107 107-
108 108-109 113-115 122-123 126-127
ring bonds :
1-12 1-2 2-3 3-4 4-26 6-7 6-126 7-8 8-17 9-13 9-10 10-11 10-16 11-12
13-14 13-19 14-15 15-16 17-18 18-19 26-27 26-28 27-28 27-125 31-32 31-36
32-33 33-34 34-35 35-36 38-50 38-39 39-40 40-41 41-64 43-44 43-65 44-45
45-46 46-55 47-51 47-48 48-49 48-54 49-50 51-52 51-57 52-53 53-54 55-56

56-57 64-65 64-66 65-66 70-71 70-75 71-72 72-73 73-74 74-75 78-90 78-79
79-80 80-81 81-104 83-84 83-105 84-85 85-86 86-95 87-91 87-88 88-89 88-
94 89-90 91-92 91-97 92-93 93-94 95-96 96-97 104-105 109-110 109-114
110-111 111-112 112-113 113-114 125-126
exact/norm bonds :
1-12 1-2 2-3 3-4 4-20 4-26 5-8 6-7 6-126 7-8 8-17 9-13 9-10 10-11 10-
16 11-12 13-14 13-19 14-15 15-16 17-18 18-19 26-27 26-28 27-28 27-125
31-32 31-36 32-33 33-34 34-35 35-36 38-50 38-39 39-40 40-41 41-58 41-64
42-46 43-44 43-65 44-45 45-46 46-55 47-51 47-48 48-49 48-54 49-50 51-52
51-57 52-53 53-54 55-56 56-57 64-65 64-66 65-66 70-71 70-75 71-72 72-73
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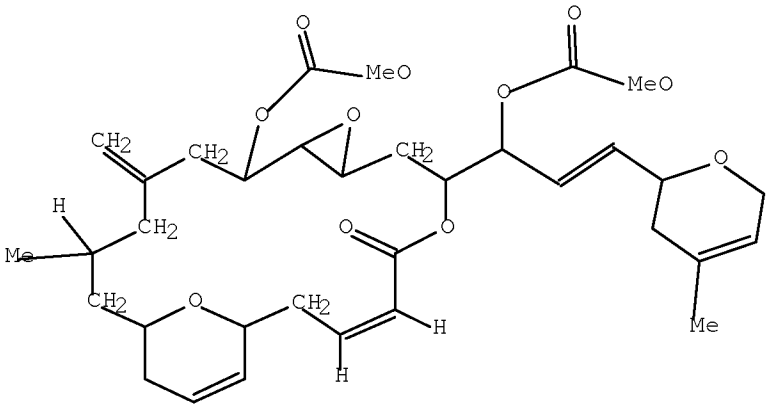
85 84-106 85-86 86-95 87-91 87-88 88-89 88-94 89-90 91-92 91-97 92-93
93-94 95-96 96-97 104-105 106-107 109-110 109-114 110-111 111-112 112-113
113-114 125-126 126-127
exact bonds :
2-21 6-29 12-22 12-25 17-24 18-23 29-30 30-31 35-37 39-59 44-67 50-60
50-63 55-62 56-61 58-77 67-68 68-69 69-70 74-76 79-99 90-100 90-103 95-
102 96-101 98-121 107-108 108-109 113-115 122-123

G2:[*1],[*2],[*3]

G3:CH2,[*4]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:CLASS 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:Atom 27:Atom
28:Atom 29:CLASS 30:CLASS 31:Atom 32:CLASS 33:CLASS 34:CLASS 35:Atom
36:Atom 37:CLASS 38:Atom 39:Atom 40:Atom 41:Atom 42:CLASS 43:Atom 44:Atom
45:Atom 46:Atom 47:Atom 48:Atom 49:Atom 50:Atom 51:Atom 52:Atom 53:Atom
54:Atom 55:Atom 56:Atom 57:Atom 58:CLASS 59:CLASS 60:CLASS 61:CLASS
62:CLASS 63:CLASS 64:Atom 65:Atom 66:Atom 67:CLASS 68:CLASS 69:CLASS
70:Atom 71:CLASS 72:CLASS 73:CLASS 74:Atom 75:Atom 76:CLASS 77:CLASS
78:Atom 79:Atom 80:Atom 81:Atom 82:CLASS 83:Atom 84:Atom 85:Atom 86:Atom
87:Atom 88:Atom 89:Atom 90:Atom 91:Atom 92:Atom 93:Atom 94:Atom 95:Atom
96:Atom 97:Atom 98:CLASS 99:CLASS 100:CLASS 101:CLASS 102:CLASS 103:CLASS
104:Atom 105:Atom 106:CLASS 107:CLASS 108:CLASS 109:Atom 110:CLASS 111:CLASS
112:CLASS 113:Atom 114:Atom 115:CLASS 120:CLASS 121:CLASS 122:CLASS
123:CLASS 125:Atom 126:Atom 127:CLASS

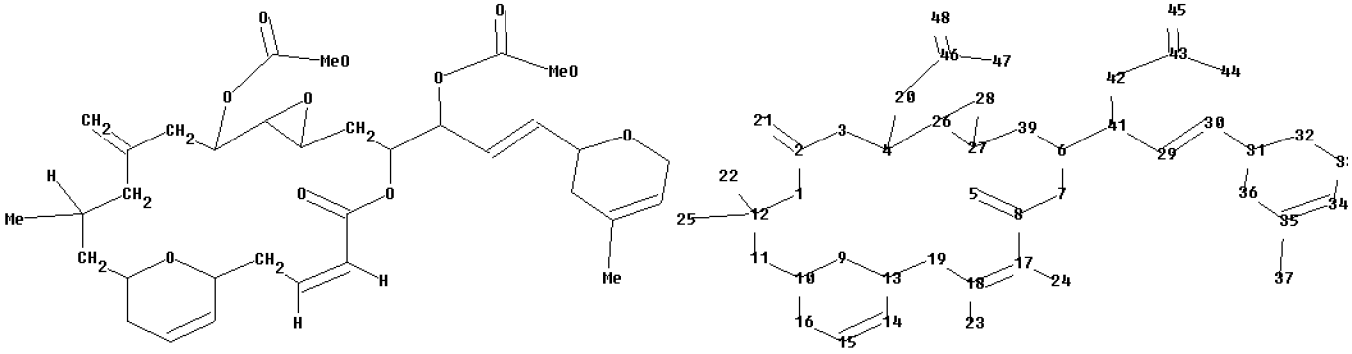
L6 STR



G1
G2
G3 CH2

Structure attributes must be viewed using STN Express query preparation.

Uploading L6.str



chain nodes :
5 20 21 22 23 24 25 29 30 37 41 42 43 44 45 46 47 48
ring nodes :
1 2 3 4 6 7 8 9 10 11 12 13 14 15 16 17 18 19 26 27 28 31 32 33 34 35 36 39
chain bonds :
2-21 4-20 5-8 6-41 12-22 12-25 17-24 18-23 20-46 29-30 29-41 30-31 35-37 41-42 42-43 43-44 43-45 46-47 46-48
ring bonds :
1-12 1-2 2-3 3-4 4-26 6-39 6-7 7-8 8-17 9-13 9-10 10-11 10-16 11-12 13-14 13-19 14-15 15-16 17-18 18-19 26-27 26-28 27-28 27-39 31-32 31-36 32-33 33-34 34-35 35-36
exact/norm bonds :
1-12 1-2 2-3 3-4 4-20 4-26 5-8 6-39 6-7 7-8 8-17 9-13 9-10 10-11 10-16 11-12 13-14 13-19 14-15 15-16 17-18 18-19 20-46 26-27 26-28 27-28 27-39 31-32 31-36 32-33 33-34 34-35 35-36 41-42 42-43 43-45 46-48
exact bonds :
2-21 6-41 12-22 12-25 17-24 18-23 29-30 29-41 30-31 35-37 43-44 46-47

G2

G3:CH2

```
Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:CLASS  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom
20:CLASS  21:CLASS  22:CLASS  23:CLASS  24:CLASS  25:CLASS  26:Atom  27:Atom
28:Atom  29:CLASS  30:CLASS  31:Atom  32:CLASS  33:CLASS  34:CLASS  35:Atom
36:Atom  37:CLASS  39:Atom  41:CLASS  42:CLASS  43:CLASS  44:CLASS  45:CLASS
46:CLASS  47:CLASS  48:CLASS



L9           21 SEA FILE=REGISTRY SUB=L2 SSS FUL (L3 OR L4 OR L5 OR L6)
L10          98 SEA FILE=REGISTRY SPE=ON  ABB=ON  L2 NOT L9



     (FILE 'HOME' ENTERED AT 09:08:15 ON 10 MAR 2009)
                D SAVED

     FILE 'REGISTRY' ENTERED AT 09:08:50 ON 10 MAR 2009
                ACT CHA870FULL/A
               ---------
L1               STR
L2           119 SEA SSS FUL L1
               ---------
L3               STRUCTURE UPLOADED
L4               STRUCTURE UPLOADED
L5               STRUCTURE UPLOADED
L6               STRUCTURE UPLOADED
L7             2 SEA SUB=L2 SSS SAM (L3 OR L4 OR L5 OR L6)
                D SCAN
L8            83 SEA SUB=L2 SSS FUL (L3 OR L4 OR L5 OR L6) EXTEND
L9            21 SEA SUB=L2 SSS FUL (L3 OR L4 OR L5 OR L6)
                SAVE TEMP L9 CHA870SUB1/A
L10           98 SEA SPE=ON  ABB=ON  L2 NOT L9
                SAVE TEMP L10 CHA870SUB2/A
                D SAVED
L11            0 SEA SPE=ON  ABB=ON  JOHANNES C?/AU
L12            0 SEA SPE=ON  ABB=ON  LI X?/AU
L13            0 SEA SPE=ON  ABB=ON  PESANT M?/AU
L14            0 SEA SPE=ON  ABB=ON  ZHAO H?/AU
L15            0 SEA SPE=ON  ABB=ON  AKASAKA K?/AU
L16            0 SEA SPE=ON  ABB=ON  FANG F?/AU

     FILE 'CAPLUS' ENTERED AT 09:14:14 ON 10 MAR 2009
L17           26 SEA SPE=ON  ABB=ON  L10
L18           73 SEA SPE=ON  ABB=ON  JOHANNES C?/AU
L19        59001 SEA SPE=ON  ABB=ON  LI X?/AU
L20           12 SEA SPE=ON  ABB=ON  PESANT M?/AU
L21        13399 SEA SPE=ON  ABB=ON  ZHAO H?/AU
L22          644 SEA SPE=ON  ABB=ON  AKASAKA K?/AU
L23         2248 SEA SPE=ON  ABB=ON  FANG F?/AU
                E GALLAGHER/AU
                E GALLAGHER BR/AU
                E GALLAGHER JR/AU
L24          356 SEA SPE=ON  ABB=ON  GALLAGHER B?/AU
L25          130 SEA SPE=ON  ABB=ON  L2
L26            4 SEA SPE=ON  ABB=ON  L25 AND (L18 OR L19 OR L20 OR L21 OR L22
```

```
               OR L23 OR L24)
               D SAVED

     FILE 'REGISTRY' ENTERED AT 09:16:19 ON 10 MAR 2009
               ACT CHA870REG1/A
               ---------
L27           1 SEA SPE=ON  ABB=ON  115268-43-4
               ---------
               ACT CHA870REG2/A
               ---------
L28           1 SEA SPE=ON  ABB=ON  352208-19-6
               ---------
               ACT CHA870REG3/A
               ---------
L29           1 SEA SPE=ON  ABB=ON  352208-15-2
               ---------

     FILE 'CAPLUS' ENTERED AT 09:16:26 ON 10 MAR 2009
L30         123 SEA SPE=ON  ABB=ON  L27
L31           7 SEA SPE=ON  ABB=ON  L28
L32          19 SEA SPE=ON  ABB=ON  L29
L33         123 SEA SPE=ON  ABB=ON  L25 AND L30
L34           7 SEA SPE=ON  ABB=ON  L25 AND L31
L35          19 SEA SPE=ON  ABB=ON  L25 AND L32

     FILE 'REGISTRY' ENTERED AT 09:16:57 ON 10 MAR 2009
L36          98 SEA SPE=ON  ABB=ON  L10 NOT L27
L37          20 SEA SPE=ON  ABB=ON  L9 NOT L27

     FILE 'CAPLUS' ENTERED AT 09:17:45 ON 10 MAR 2009
L38          21 SEA SPE=ON  ABB=ON  L37
L39          15 SEA SPE=ON  ABB=ON  L17 AND L38

     FILE 'CAPLUS' ENTERED AT 09:19:43 ON 10 MAR 2009
               D QUE NOS L26
               D IBIB ABS HITSTR L26 1-4

     FILE 'REGISTRY' ENTERED AT 09:20:08 ON 10 MAR 2009
               D STAT QUE L10

     FILE 'CAPLUS' ENTERED AT 09:20:25 ON 10 MAR 2009
               D QUE NOS L17
L40          24 SEA SPE=ON  ABB=ON  L17 NOT L26
               D IBIB ABS HITSTR L40 1-24

     FILE 'REGISTRY' ENTERED AT 09:21:06 ON 10 MAR 2009
               D QUE NOS L37

     FILE 'CAPLUS' ENTERED AT 09:21:21 ON 10 MAR 2009
               D QUE NOS L38
L41          19 SEA SPE=ON  ABB=ON  L38 NOT L26
L42           6 SEA SPE=ON  ABB=ON  L41 NOT L40
L43           6 SEA SPE=ON  ABB=ON  L38 NOT (L26 OR L40)
               D IBIB ABS HITSTR 1-6
L44          13 SEA SPE=ON  ABB=ON  L38 AND L40
               D SCAN TI

     FILE 'REGISTRY' ENTERED AT 09:24:05 ON 10 MAR 2009
               D QUE NOS L27
               D IDE L27
```

```
     FILE 'CAPLUS' ENTERED AT 09:24:23 ON 10 MAR 2009
                D QUE NOS L30
L45          25 SEA SPE=ON  ABB=ON  L30 AND (L40 OR L38)
                D SCAN TI
                D PY L30 123

     FILE 'HOME' ENTERED AT 09:25:48 ON 10 MAR 2009
                D STAT QUE L10

=>
```